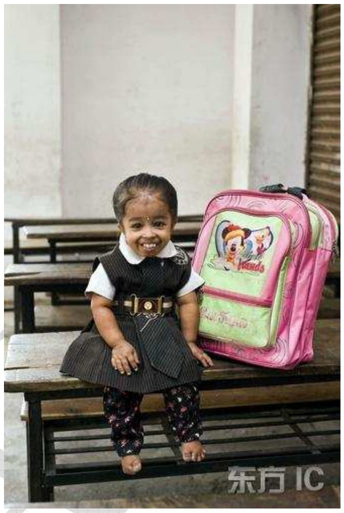
syndrome	*Heart defect*	*Other associated defect*
Down syndrome **Trisomy 21**	**30%-40% have congenital heart disease .** **The common defect are AVSD , VSD , ASD**	**10% have GIT anomalies , congenital hypothyroidism , polycythaemia at birth , they have 10% to 18% chances to have leukaemia compared to unaffected individual .**
Edward syndrome trisomy 18	**VSD , Double outlet right ventricle .**	**It's lethat condition , less than 10% of affected survive to their first birthday , developmental delay , rocker bottom feet , crossed index finger.**
Patau syndrome trisomy 13	**Double outlet right ventricle , VSD , (PDA , ASD) can be feature also .**	**8.6% of affected infant will survive beyond their first birthday. Holoprasencephaly , renal anomalies , midline facial cleft .**
William syndrome **Deletion in 7q 11.23 & elastin gene EIN gene abnormality on long arm chromsome 7 .**	**Supra valve aortic stenosis ,** **Periphral pulmonary artery stenosis .**	**Coktail party chatter , hypertolerism , hypercalcaemia , carp shape mouth , they have been described to have elfin like face , 10% of children who are affected with william syndrome have classical feature of autism , patients often have remarkable musical ability , a few cases are inherited from a parent to child in AD-like pattern .**
Noonan 12q	**HOCM , Pulmonary stenosis , ASD**	**Short stature , almond shape eye , shallow orbits , shield shape chest , widely spaced nipple .**
Turner 45XO	**45% have corcation of aorta , bicusped aortic valve may develop later in life , poststenotic aortic dilitation with aneurysm may develop**	**Infertility , short stature , shield shape chest with wide spaced nipple ,horseshoe kidney & duplication of collecting system seen im more than half patients.**
DiGeorge Syndrome 22q 11.2	**Common arterial trunk & contruncal anomalies , interupted aortic arch VSD , TOF**	**Hypoplasia of thymus and parathyroid gland , mild to moderate mental retardation , cleft palate , small jaw , pinched nose , hypertolerism renal anomalies present in 20% of patients .**

Allagille syndrome	Periphral pulmonary stenosis	Prominent forhead , deep wide set eye , small chin , butterfly vertebra , intrahepatic biliary hypoplasia , embryotoxon slit lamp of cornea , high pitche voice , renal abnormalities .
VACTERL	VSD , coarctation of aorta , TOF , PDA	
CHARGE	VSD , TOF	Colboma , Heart disease , Atresia of the chonace , Retardation , Renal , Genital malformation , Growth retardation , Ear malformation .
Cri Du Chat. 5P	VSD ASD	_
Tuberos sclerosis TSC1 & TSC2 gene defect	Cardio-rhabdomyoma which regress with age .	_
HOCM multiple gene	Commonest ASD VSD , obstruction of left ventricle associated with Noonan syndrome	_
Pentalogy of cantrell	TOF	Absent sternum , absent pericardium , absent diaphragam Ectopic heart , absent of normal heart .
Holt-oram , TAR , fanconi 12q2	ASD	Radail aplasia , limb abnormalities .

ACHONDROPLASIA; ACH / *OMIM 2010*

ORIGINAL



INHERITANCE:

Autosomal dominant

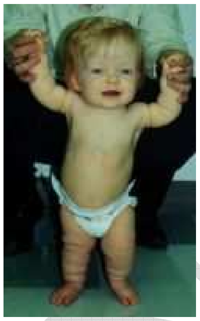
GROWTH :

Height

Short-limb dwarfism identifiable at birth

Mean male adult height, 131cm

Mean female height, 124 cm



HEAD AND NECK:

Head

Frontal bossing

Megalencephaly

Face

Midface hypoplasia

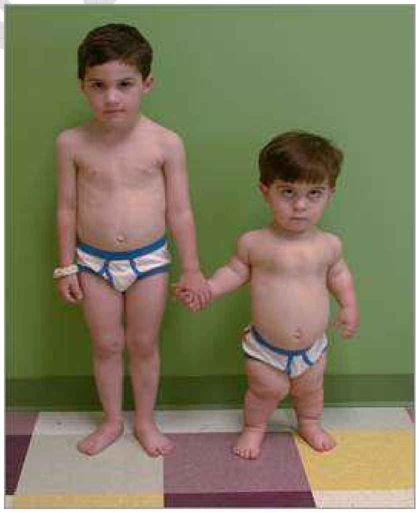
Ears

Recurrent otitis media in infancy and childhood

Conductive hearing loss

Nose

Low nasal bridge



RESPIRATORY:

Upper airway obstruction

SKELETAL:

Generalized joint laxity

Skull

Foramen magnum stenosis

Spine

Lumbar kyphosis in infancy

Exaggerated lumbar lordosis during childhood and adulthood

Congenital spinal stenosis due to short pedicles, especially lumbar

Progressive interpediculate narrowing in lumbar spine

Pelvis

Dysplastic ilium

Narrow sacroiliac groove

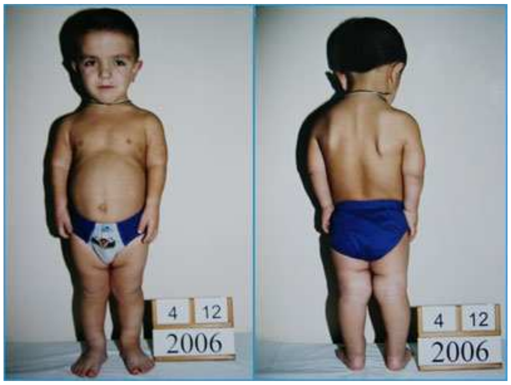
Flat rooted acetabulae

Limbs

Bowing of legs

Rhizomelic shortening

Short femoral neck



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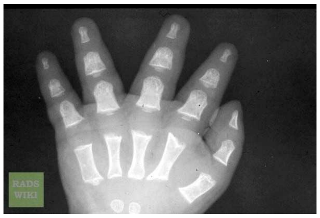
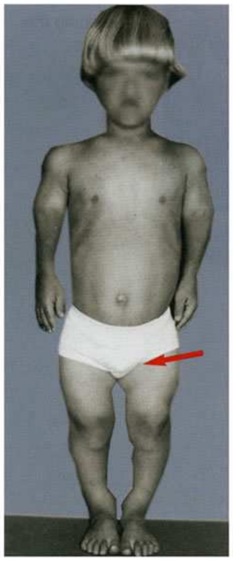
Metaphyseal flaring
Limited elbow and hip extension

Hands

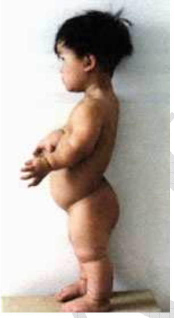
Brachydactyly
Trident hand





NEUROLOGIC:

Hydrocephalus, occasional
Hypotonia in infancy and early childhood
Brain stem compression
Delayed motor development



MISCELLANEOUS:

Autosomal dominant with complete penetrance
80% cases new mutations
99+% of the mutations are FGFR3, G380R (134934.0001)
Paternal age effect

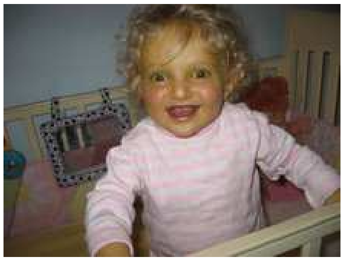
MOLECULAR BASIS:

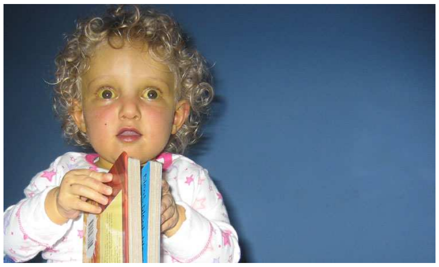
Caused by mutation in the fibroblast growth factor receptor-3 gene (FGFR3, 134934.0001)

ORIGINAL

MOSTAFA ELBABA

ALAGILLE SYNDROME; ALGS / *OMIM 2010*





INHERITANCE:

Autosomal dominant

GROWTH:

Failure to thrive

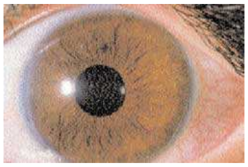
HEAD AND NECK:

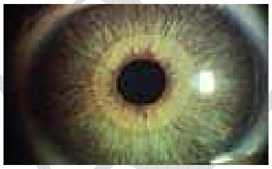
Face

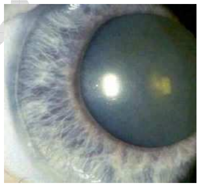
Broad forehead
Triangular face
Prominent zygomatic arch

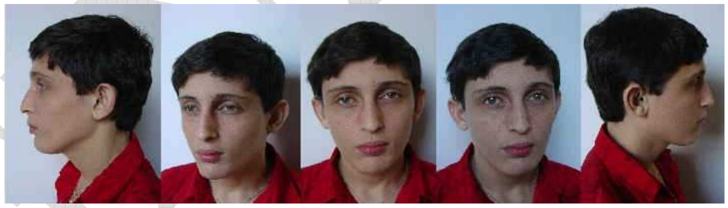
Eyes

Deep-set eyes
Posterior embryotoxon
Anterior chamber anomalies
Eccentric or ectopic pupils
Chorioretinal atrophy
Retinal pigment clumping
Axenfeld anomaly
Choroidal folds
Strabismus
Myopia
Anomalous optic disc







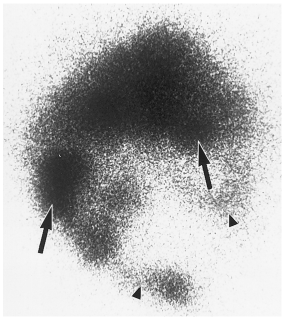


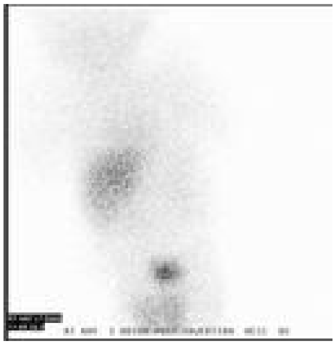
Nose

Long nose with bulbous tip

CARDIOVASCULAR:

Peripheral pulmonary artery stenosis
Atrial septal defect
Ventricular septal defect
Coarctation of aorta





CHEST:

Ribs, sternum, clavicles, and scapulae

Rib anomalies

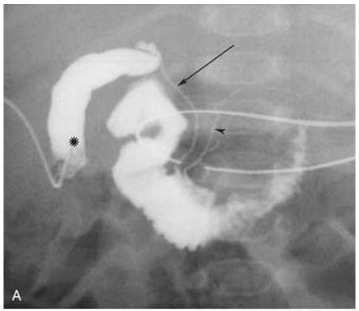
ABDOMEN:

Liver

Cholestasis
Intrahepatic duct deficiency

Biliary tract

Extrahepatic duct involvement



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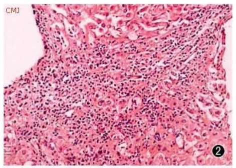
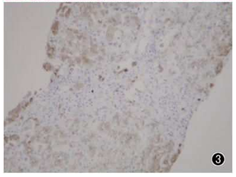




ORIGINAL

SKELETAL:

Spine
Vertebral anomalies
Butterfly vertebral arch
Hemivertebrae
Limbs
Short ulnae
Hands
Short distal phalanges

NEUROLOGIC:

Central nervous system
Mild mental retardation, occasional
Learning disability
Peripheral nervous system
Absent deep tendon reflexes

GENITOURINARY:

Kidneys
Renal dysplasia
Renal mesangiolipidosis
Medullary cystic disease

NEOPLASIA:

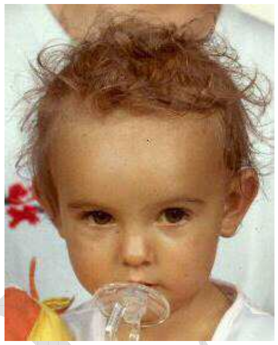
Hepatocellular carcinoma
Papillary thyroid carcinoma

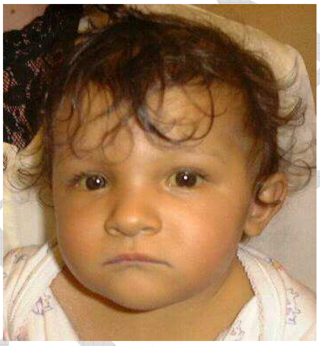
LABORATORY:

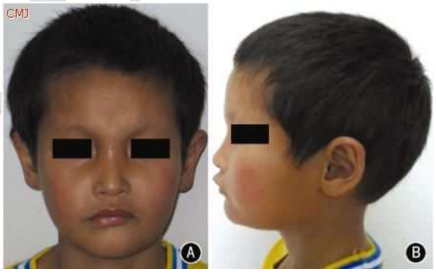
Hypercholesterolemia
Hypertriglyceridemia
Elevated transaminases
Abnormal liver function tests

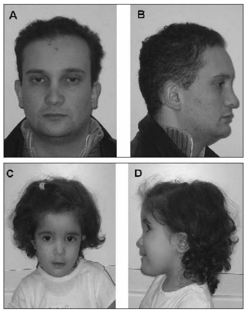
MOLECULAR:

Caused by mutation in the jagged 1 gene (JAG1, 601920.0001)









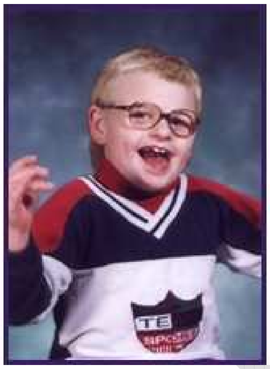
MOSTAFA ELBABA

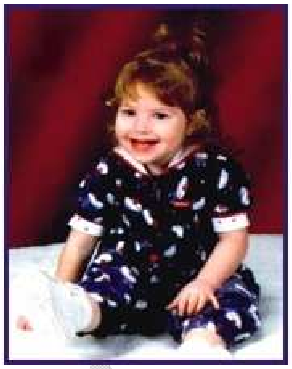
ORIGINAL

ANGELMAN SYNDROME; AS / *OMIM 2010*

INHERITANCE:

Isolated cases





GROWTH:

Obesity (older children)

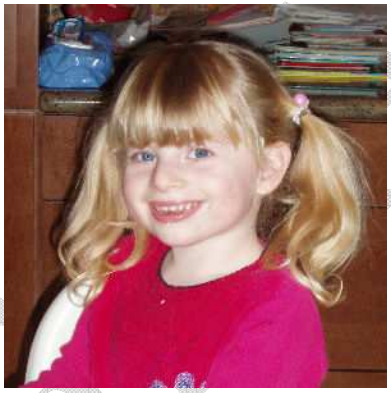
HEAD AND NECK:

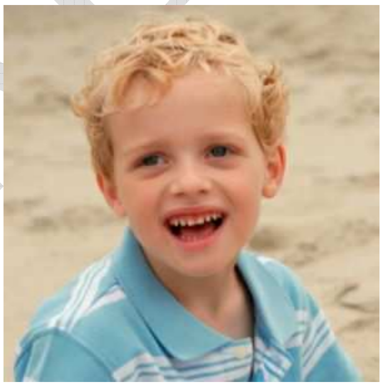
Head

Microcephaly, postnatal
Brachycephaly
Flat occiput
Occipital groove

Face

Prognathia





Eyes

Strabismus

Mouth

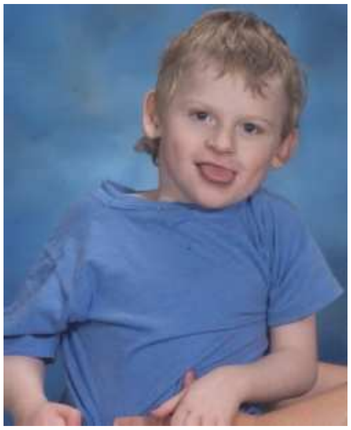
Protruding tongue
Macrostomia
Excessive drooling

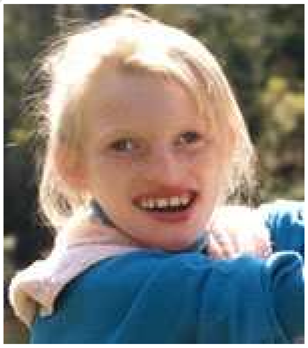
Eyes

Decreased pigmentation of choroid and iris

Teeth

Widely spaced teeth





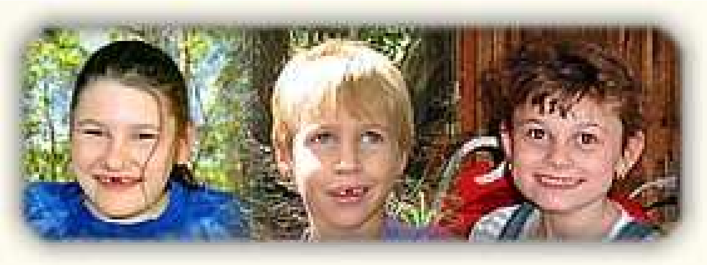
ABDOMEN:

Gastrointestinal

Feeding difficulties in neonatal period
Excessive chewing/mouthing behaviors
Abnormal food-related behaviors
Constipation

SKELETAL:

Scoliosis



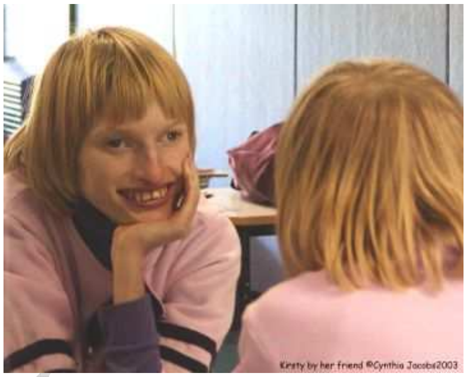
SKIN, NAILS, HAIR:

Hypopigmentation (seen only in deletion cases)

NEUROLOGIC:

Central nervous system

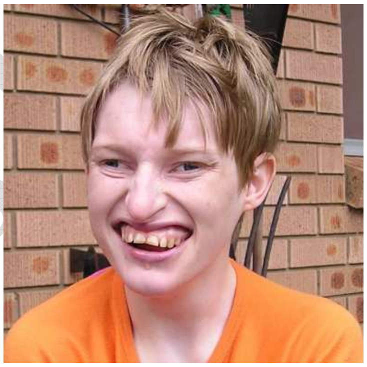
Developmental delay


Kirsty by her friend ©Cynthia Jacobs2003

Severe mental retardation
Absent speech
Ataxia with jerky arm movements
Wide-based gait
Clumsiness, unsteadiness
Tremor of limbs
Hypotonia
Seizures
Hyperreflexia
Characteristic arm position with wrist and elbow flexion
Abnormal sleep-wake cycles
Decreased need for sleep
Characteristic electroencephalogram (EEG) discharges
Mild cortical atrophy on CT or MRI

Behavioral/psychiatric manifestations

Paroxysmal laughter
Easily excitable
Attraction to/fascination with water, crinkly items (paper, plastic)

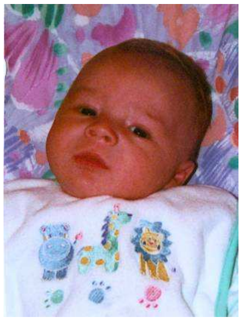


MISCELLANEOUS:

Onset between 6 and 12 months of age
Increased sensitivity to heat
70% due to de novo maternal deletion of 15q11.2-q13
2% due to paternal uniparental disomy of 15q11.2-q13
2-3% due to imprinting defects
25% due to mutations in UBE3A (601623)

MOLECULAR:

Caused by mutation in the ubiquitin protein ligase E3A gene (UBE3A, 601623.0001)

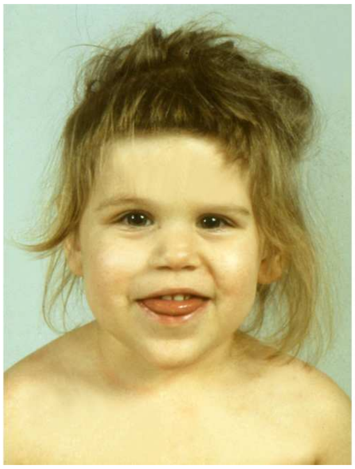


MOSTAFA ELBABA

ORIGINAL

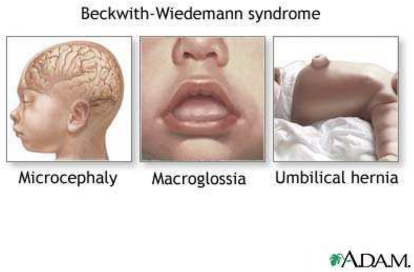
BECKWITH-WIEDEMANN SYNDROME/ *BWS OMIM 2008*

Clinical Synopsis

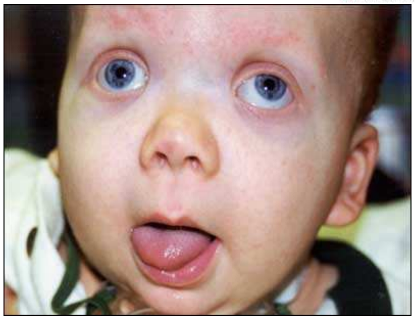


INHERITANCE :
Autosomal dominant

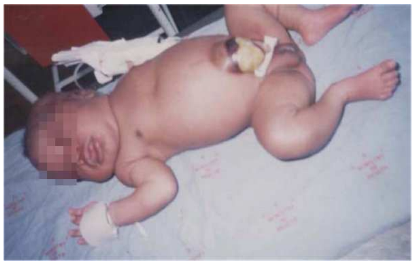
GROWTH :
Height
Average birth length, 52.6cm
Growth parallels curve at or above 95%
Weight
Average birth weight 4kg
Other
Generalized overgrowth
Hemihypertrophy



HEAD AND NECK :
Head
Metopic ridge
Large fontanelle
Prominent occiput



Face
Coarse facial features
Eyes
Prominent
Ears
Linear ear lobe creases
Posterior helical indentations

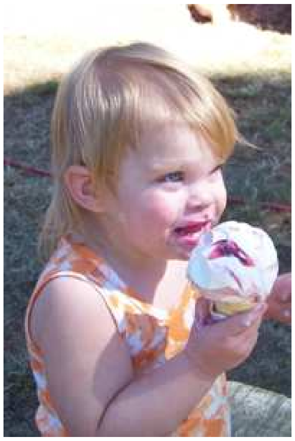


Mouth
Macroglossia

CARDIOVASCULAR :
Heart
Cardiomyopathy
Cardiomegaly

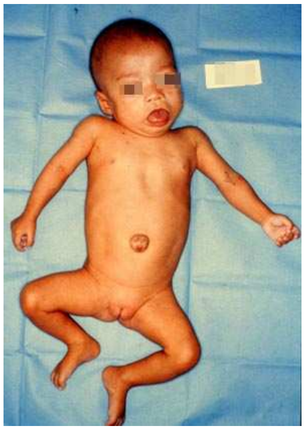
ABDOMEN :
External features
Omphalocele (exomphalos)
Diastasis recti
Liver

Hepatomegaly
Pancreas
Pancreatic hyperplasia



GENITOURINARY :
External genitalia, male
Overgrowth of external genitalia
External genitalia, female
Overgrowth of external genitalia
Internal genitalia, male
Cryptorchidism
Kidneys
Renal medullary dysplasia
Large kidneys

SKELETAL :
Advanced bone age, most pronounced during first 4 years



METABOLIC :
Neonatal hypoglycemia

ENDOCRINE FEATURES :
Adrenocortical cytomegaly
Pituitary amphophil hyperplasia

NEOPLASIA :
Wilms tumor
Hepatoblastoma
Adrenal carcinoma
Gonadoblastoma

LABORATORY ABNORMALITIES :
Caused by duplication or deletion at 11p15.5

MISCELLANEOUS :
Genetic heterogeneity
Most cases are isolated
Imprinting at 11p15.5

DIAGNOSIS

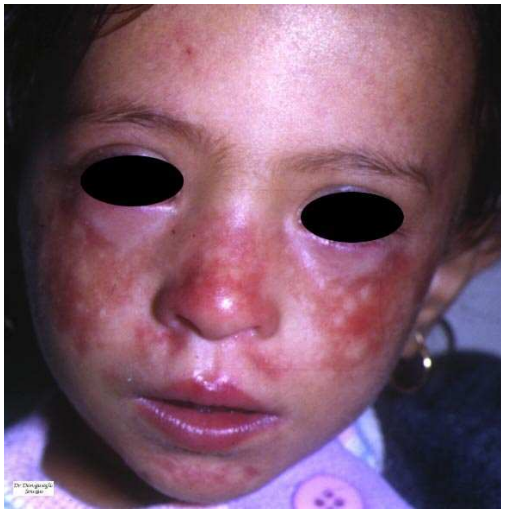
Diagnosis is based on clinical findings. A careful cytogenetic analysis of the 11p15 region is recommended. Prenatal diagnosis by ultrasonography is possible.

MOLECULAR GENETICS

1. **Mutation in the cyclin-dependent kinase inhibitor 1C gene (CDKN1C, 600856.0001)**
2. **Mutation in the nuclear receptor binding SET domain protein 1 (NSD1, 606681.0011)**
3. **Mutation in the H19 gene (H19, 103280.0001)**
4. **Mutation in the KCNQ1-overlapping transcript 1 gene (KCNQ10T1, 604115.0001)**

BLOOM SYNDROME; BLM

Clinical Synopsis



INHERITANCE :
- Autosomal recessive

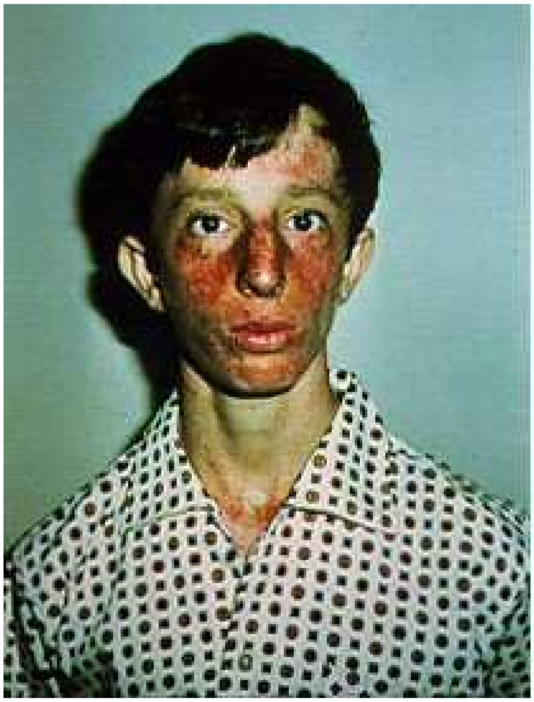
GROWTH :
- **Height**
- Average adult male height 151cm
- Average adult female height 144cm
- **Other**
- Prenatal onset growth retardation
- Growth failure

HEAD AND NECK :
- **Head**
- Dolichocephaly
- Microcephaly
- **Face**
- Narrow
- Malar hypoplasia
- **Ears**
- Prominent ears
- **Nose**
- Prominent nose
- **Teeth**
- Absent upper lateral incisors

RESPIRATORY :
- **Airways**
- Bronchiectasis
- **Lung**
- Chronic lung disease

GENITOURINARY :
- **Internal genitalia, male**
- Azoospermia
- Cryptorchidism
- **Internal genitalia, female**
- Reduced fertility in females

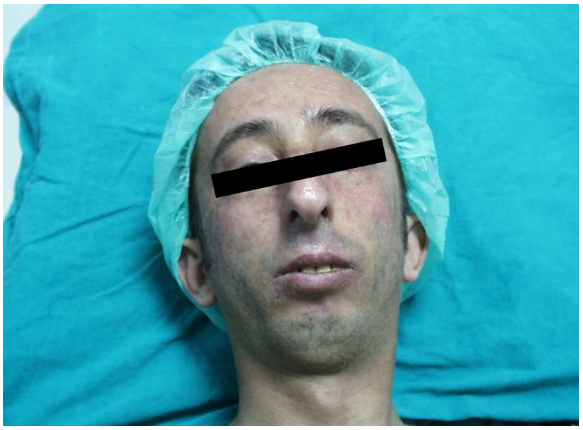
SKELETAL :
- **Hands**



Syndactyly
Polydactyly
Fifth finger clinodactyly

SKIN, NAILS, HAIR :

Facial telangiectasia in butterfly midface distribution (exacerbated by sun)
Spotty hypopigmentation
Spotty hyperpigmentation
Cafe-au-lait spots
Hypertrichosis
Photosensitivity



NEUROLOGIC :

Central nervous system
Mild mental retardation in some
Learning disability

VOICE :

High-pitched

ENDOCRINE FEATURES :

Noninsulin-dependent diabetes mellitus

IMMUNOLOGY :

Immunoglobulin deficiency (IgA, IgG, IgM)
Impaired lymphocyte proliferation response to malignancy

NEOPLASIA :

Leukemia
Lymphoma
Adenocarcinoma
Squamous cell carcinoma
Hypersensitivity to chemotherapy

LABORATORY ABNORMALITIES :

High sister chromatid exchange (SCE) rate
SCE normal in heterozygotes
Increased chromosomal breakage
Decreased IgA, IgG, IgM

MISCELLANEOUS :

Life-threatening infections
Predisposition to neoplasia

MOLECULAR BASIS

Caused by mutations in the RecQ protein-like 3 gene (RECQL3, 604610.0001)

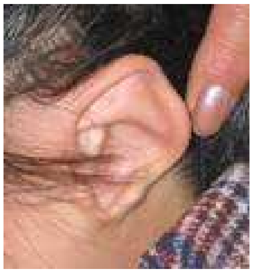
CHARGE Association / *OMIM2008*

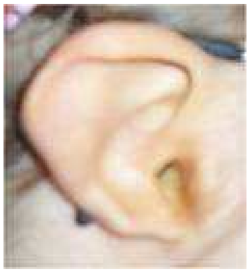
HALL-HITTNER SYNDROME; HHS

Clinical Synopsis

INHERITANCE :

Autosomal dominant.Isolated cases. Caused by mutation in the chromodomain helicase DNA-binding protein 7 gene (CHD7, 608892.0001)





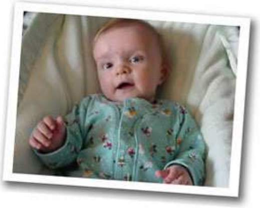
GROWTH :

Postnatal growth retardation

HEAD AND NECK :

Head

Microcephaly



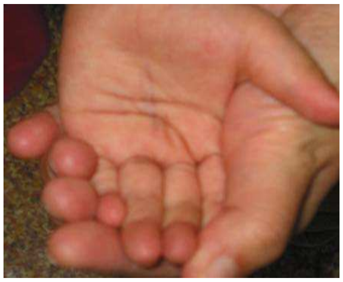
Face

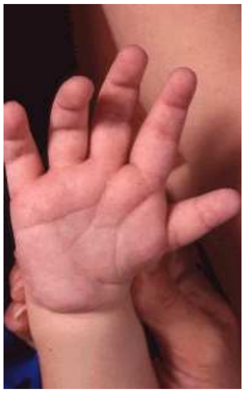
Square face

Malar flattening

Micrognathia

Facial asymmetry





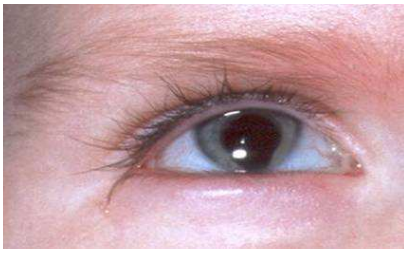
Ears

Small ears

Lop ears

Deafness (sensorineural or mixed sensorineural and conductive)

Mondini defect



Eyes

Colobomas (iris, choroid, retina, disk, and optic nerve)

Anophthalmia

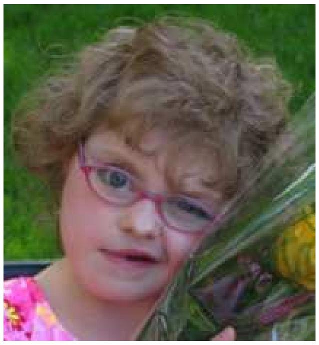
Ptosis

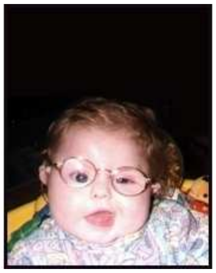
Hypertelorism

Down-slanting palpebral fissures

Nose

Posterior choanal atresia (membranous and/or bony)





Mouth

Cleft palate

Cleft lip

CARDIOVASCULAR :

Heart

Tetralogy of Fallot

Atrial septal defect
Double-outlet right ventricle

CHEST :

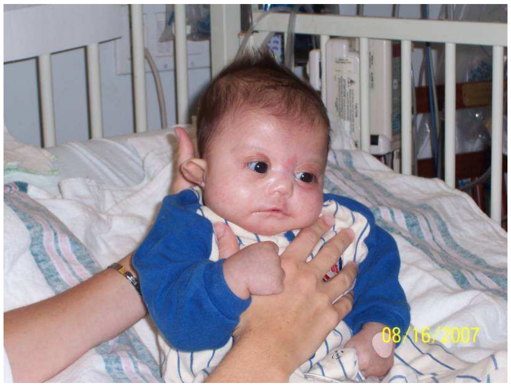
Ribs, sternum, clavicles, and scapulae
Rib anomalies

ABDOMEN :

External features
Umbilical hernia
Omphalocele
Gastrointestinal
Tracheoesophageal fistula
Anal atresia
Anal stenosis
Poor feeding

GENITOURINARY :

Delayed pubertal development
External genitalia, male
Micropenis
External genitalia, female
Hypoplastic labia
Internal genitalia, male
Cryptorchidism
Kidneys
Horseshoe kidney
Hydronephrosis

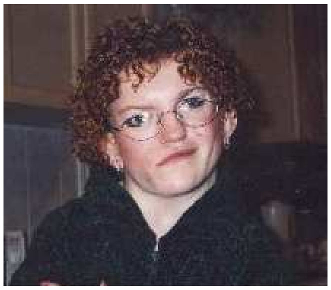


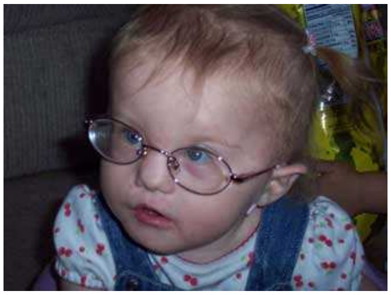
NEUROLOGIC :

Central nervous system
Mental retardation
Peripheral nervous system
Facial palsy
Dysphagia

ENDOCRINE FEATURES :

Growth hormone deficiency
Parathyroid hypoplasia



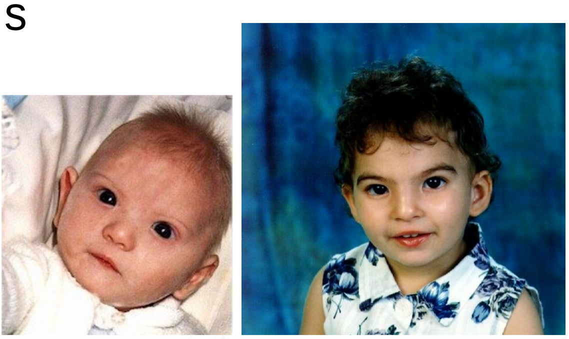


MISCELLANEOUS :

CHARGE acronym (Coloboma, Heart defect, Atresia choanae, Retarded growth and development, Genital hypoplasia, Ear anomalies/deafness)

CRI-DU-CHAT / *OMIM 2008*

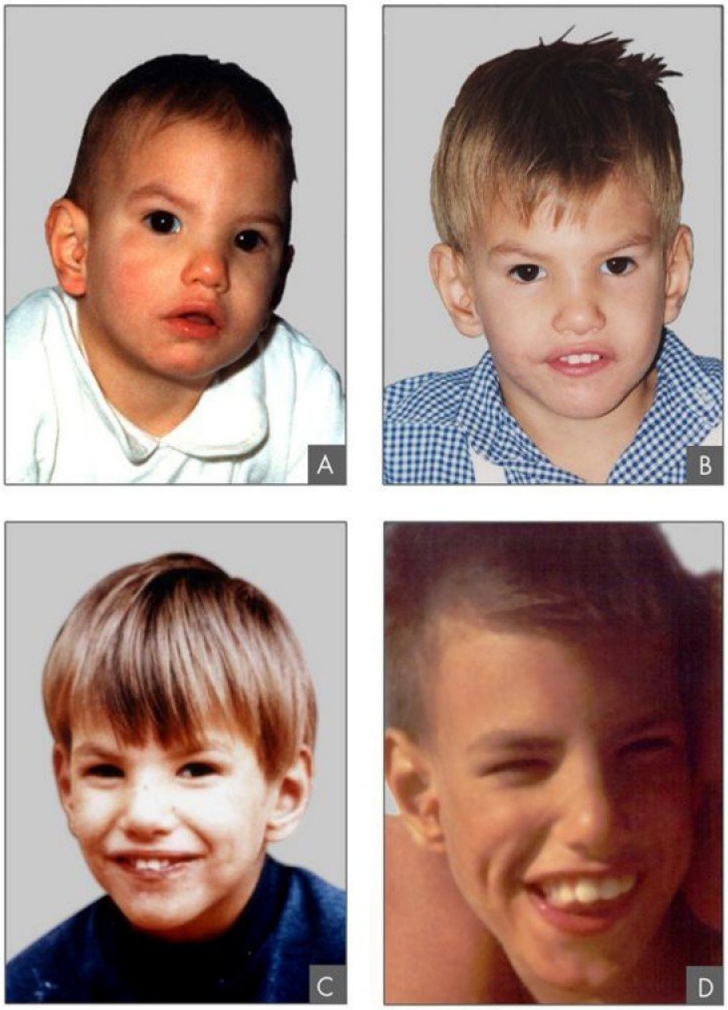
Clinical Synopsis



INHERITANCE :

Deletion of the short arm of chromosome 5

Most characteristic features in newborn is a high-pitched cat-like cry



GROWTH :
- Failure to thrive in infancy

HEAD AND NECK :
- HEAD
- Microcephaly

- Face
- Round face
- Micrognathia

- Ears
- Low-set ears

- Eyes
- Hypertelorism
- Epicanthal folds

SKELETAL :
- Vertebral abnormalities

MUSCLE, SOFT TISSUE :
- Hypotonia

NEUROLOGIC :
- Mental retardation

Behavioral/psychiatric manifestations
- Severe psychomotor retardation
- Destructive behavior, self mutilation,aggression

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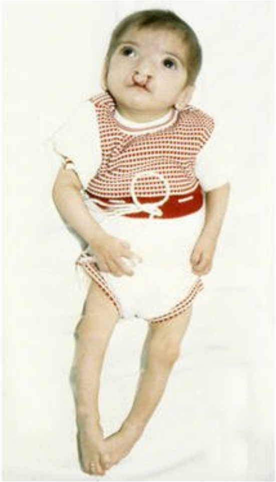
Last update: 28 September 2008



MISCELLANEOUS :

-One of the most common human deletion syndromes, incidence 1 in 20,000 to 1 in 50,000 births

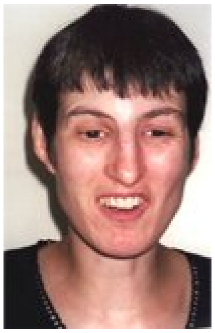
-Deletions can vary in size from involving only band to all short arm

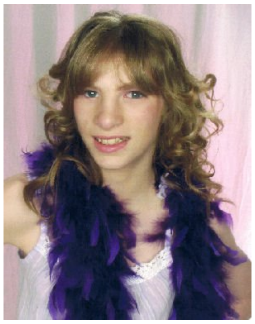
-Majority of deletions are new mutations

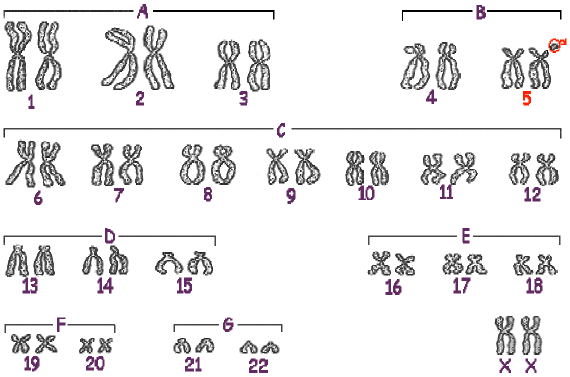
-12% unbalanced translocations or recombination pericentric inversion in one of parents

-The majority die in early childhood

-With advancing age, the clinical manifestations become less striking(loss of hypertelorism and epicanthic folds, and development of a thin, narrow face with prominent nasal bridge) making diagnosis more difficult







MOLECULAR BASIS

High-pitched cry mapped to proximal 5p15.3 (probe D5S727)
Remaining features of the syndrome mapped to 5p15.2 (probe D5S721
Deletions that did not include these 2 chromosomal regions presented varying clinical phenotypes from severe mental retardation and microcephaly to a clinically normal phenotype.

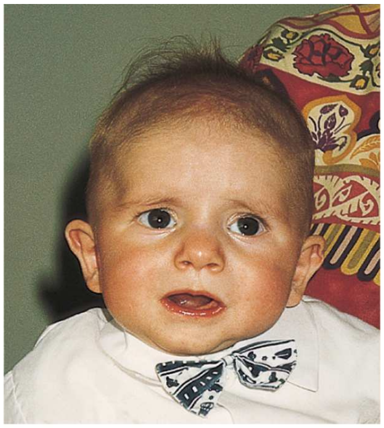
DIGEORGE SYNDROME; DGS
CHROMOSOME 22q11.2 DELETION SYNDROME
CATCH22 / *OMIM 2008*

Clinical Synopsis

INHERITANCE :
- Autosomal dominant

GROWTH :
- **Height**
- Short stature (20% of adults)
- **Weight**
- Obesity (35% of adults)

HEAD AND NECK :
- **Face**
- Micrognathia
- **Ears**
- Low-set ears
- Abnormal folded pinna
- Middle ear abnormalities
- Hearing deficits (28% of adults)
- **Eyes**
- Posterior embryotoxon
- Tortuous retinal vasculature
- Hypertelorism
- Short palpebral fissures
- Eyelid hooding
- Amblyopia
- Strabismus (15% of adults)
- Exotropia
- Esophoria
- Accommodative esotropia
- Complicated strabismus



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- **Nose**
- Blunted nose
- Short philtrum
- **Mouth**
- High arched palate

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Last update: 1 October 2008

Cleft palate
Bifid uvula

CARDIOVASCULAR :

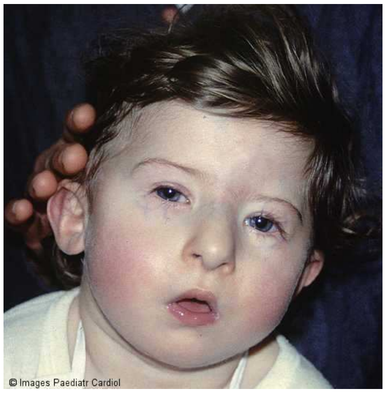
Heart
Cardiovascular malformations (26% of adults)
Tetralogy of Fallot
Truncus arteriosus
Interrupted aortic arch
Right aortic arch

Ventricular septal defect
Vascular
Patent ductus arteriosus

ABDOMEN :

External features
Umbilical hernia
Femoral hernia
Biliary tract
Cholelithiasis (19% of adults)

GENITOURINARY :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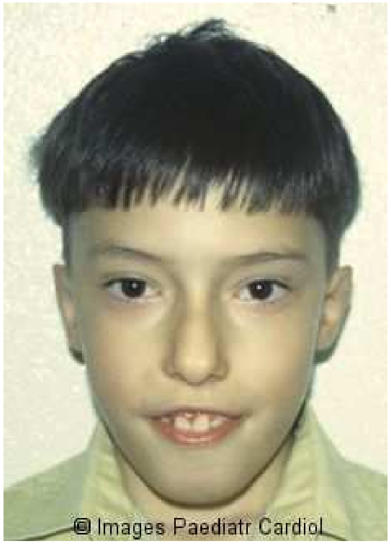
External genitalia, male
Inguinal hernia
Kidney
Unilateral renal agenesis
Renal dysplasia
Hydronephrosis

SKELETAL :

Spine
Scoliosis (47% of adults)

SKIN, NAILS, HAIR :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Skin
Severe acne (23% of adults)
Seborrhea (35% of adults)

NEUROLOGIC :

Central nervous system
Mild to moderate learning difficulties
Delayed psychomotor development
Late-onset speech development
Tetany
Seizures (40%)
Behavioral/psychiatric manifestations

- Attention deficit disorder
- Schizophrenia (22% of adults)
- Bipolar disorder

VOICE :

- Hypernasal speech

ENDOCRINE FEATURES :

- Parathyroid hypoplasia
- Parathyroid absence
- Thymic hypoplasia
- Thymic aplasia
- Accessory thyroid tissue
- Hypothyroidism (20% of adults)

IMMUNOLOGY :

- Immune defect due to a T cell deficit
- Susceptibility to infection

LABORATORY ABNORMALITIES :

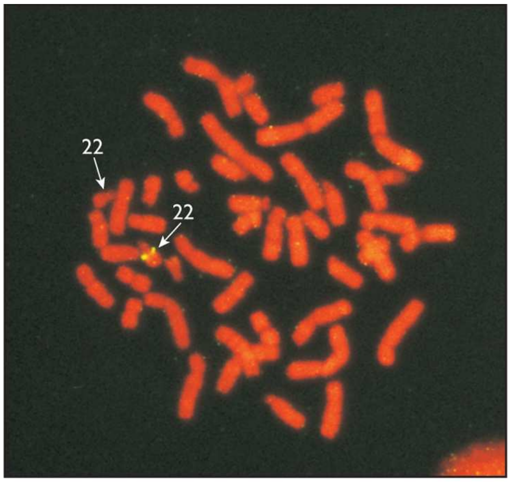
- Neonatal hypocalcemia
- Hypocalcemia (64% of adults)
- T-cell deficit
- 85-90% DGS patients have deletion of 22q11.2
- Other cytogenic abnormalities have been associated with DGS phenotype including monosomy 10p13, 11p13, and 4q21

MISCELLANEOUS :

- Incidence of approximately 1 in 5,000 live births
- Hernia occurs in 22% of adults
- Usually sporadic disorder resulting from de novo 22q11.2 deletion
- 22q11.2 deletion can present with a variety of phenotypes including velocardiofacial syndrome (192430)

MOLECULAR BASIS

A contiguous gene syndrome involving deletion of the DiGeorge syndrome chromosome region (DGCR) involving mutations in TUP-like enhancer of split 1 (TUPLE1, 600237) and DiGeorge critical region gene 2 (DGCR2, 600594)



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DOWN SYNDROME

Clinical Synopsis

INHERITANCE :
- Isolated cases

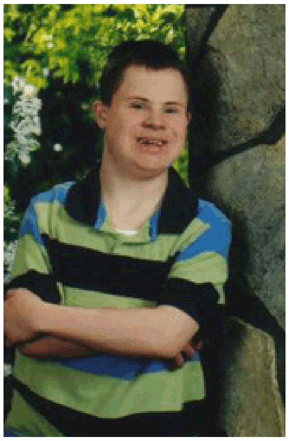
GROWTH :
- **Height**
- Short stature

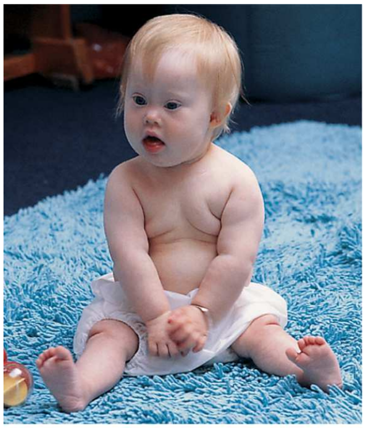
HEAD AND NECK :
- **Head**
- Brachycephaly
- **Face**
- Flat facial profile
- **Ears**
- Small ears
- Folded helix
- Conductive hearing loss
- **Eyes**
- Upslanting palpebral fissures
- Epicanthal folds
- Iris Brushfield spots
- **Mouth**
- Protruding tongue

CARDIOVASCULAR :
- **Heart**
- Congenital heart defect
- Atrioventricular canal

ABDOMEN :
- **Gastrointestinal**
- Duodenal stenosis/atresia
- Imperforate anus
- Hirschsprung disease

SKELETAL :
- **Spine**
- Atlantoaxial instability
- **Pelvis**
- Hypoplastic iliac wings
- Shallow acetabulum





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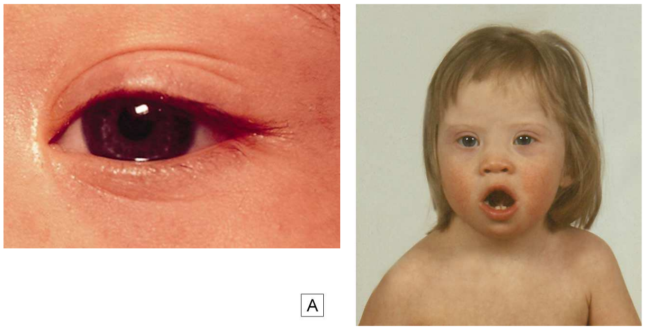

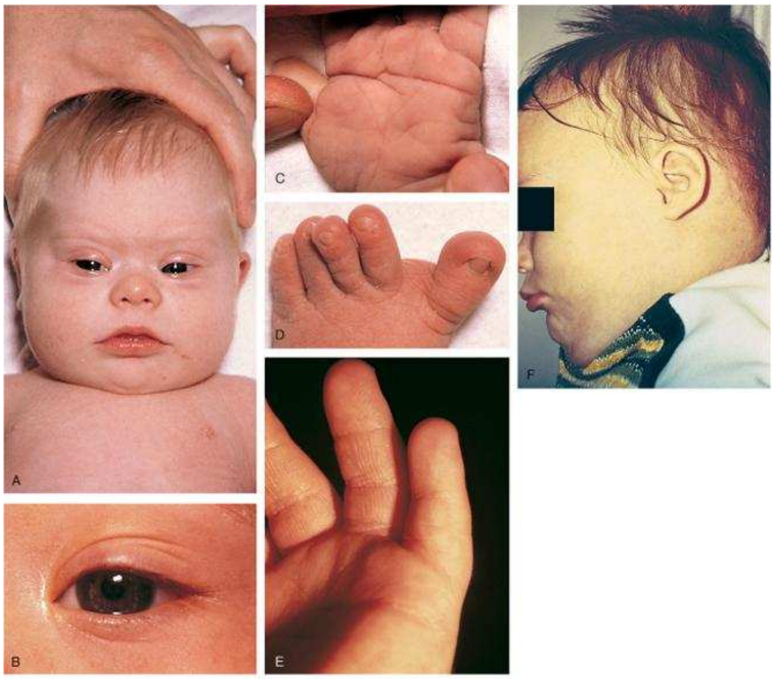

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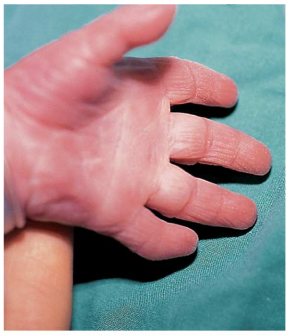
Limbs
Joint laxity
Hands
Short, broad hands
Fifth finger mid-phalanx hypoplasia
Single transverse palmar crease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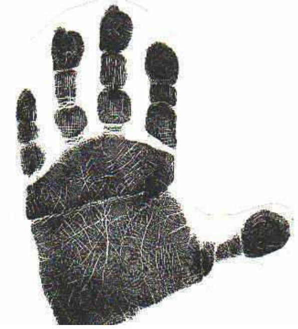
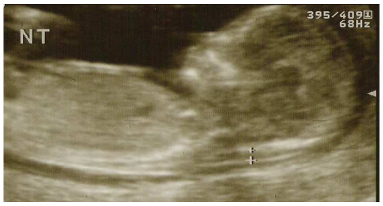


SKIN, NAILS, HAIR :
Skin

Excess nuchal skin
Single transverse palmar crease

NEUROLOGIC :
Central nervous system
Mental retardation
Alzheimer disease
Hypotonia, poor Moro reflex

ENDOCRINE FEATURES :
Hypothyroidism
HEMATOLOGY :
Leukemoid reactions



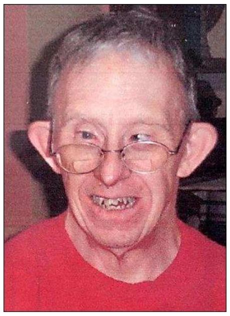
NEOPLASIA :
Leukemia (both ALL and AML)
Acute megakaryocytic leukemia
MISCELLANEOUS :
Meiotic origin >95% maternal, mostly meiosis I
Increased recurrence risk with parental translocation
Incidence, 1 in 650-1000 live births

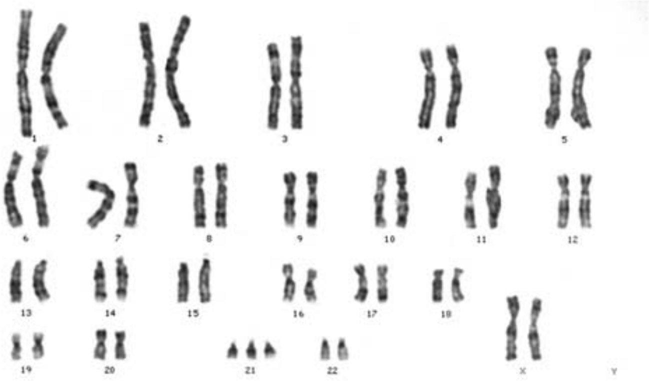
Down Syndrome newborn

MOLECULAR BASIS

Gene map locus Xp11.23, 21q22.3, 1q43

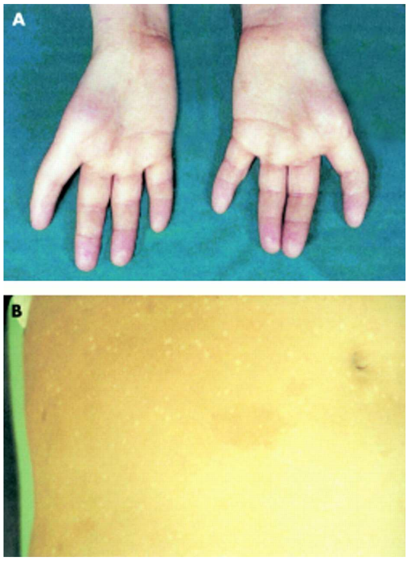
- Full trisomy 21, 94%
- Mosaic trisomy 21, 2.4%
- Translocation 21, 3.3%

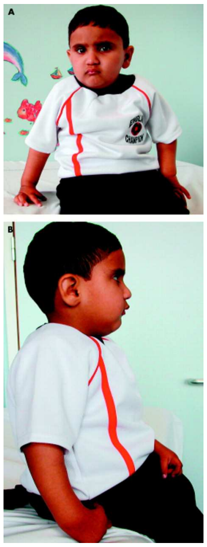




FANCONI ANEMIA; FA

Clinical Synopsis

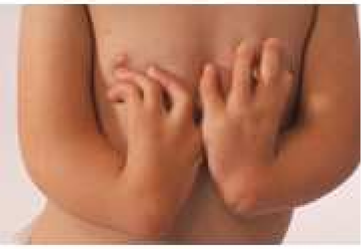




Growth :
- Low birth weight
- Small stature

Skel :
- Radial aplasia
- Thumb deformity
- Thumb aplasia
- Thumb hypoplasia
- Duplicated thumb

Heme :
- Anemia
- Neutropenia
- Thrombocytopenia
- Reticulocytopenia
- Pancytopenia
- Bleeding
- Leukemia



Skin :
- Anemic pallor
- Bruisability

- Pigmentary changes
- Hyperpigmentation
- Cafe-au-lait spots

HEENT :
- Microcephaly
- Strabismus
- Microphthalmia
- Ear anomaly
- Deafness

Cardiac :
- Congenital heart defect

GU :
- Kidney malformation
- Absent kidney

Duplicated kidney
Duplicated collecting system
Horseshoe kidney
Renal ectopia
Hypergonadotropic hypogonadism
Cryptorchidism

Neuro :

Mental retardation

Lab :

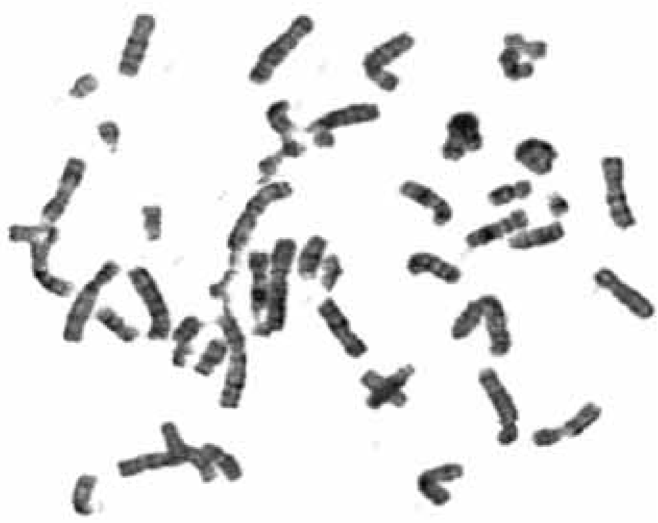
Multiple chromosomal breaks
Chromosomal breakage induced by diepoxybutane (DEB), and mitomycin C
Deficient excision of UV-induced pyrimidine dimers in DNA
Prolonged G2 phase of cell cycle

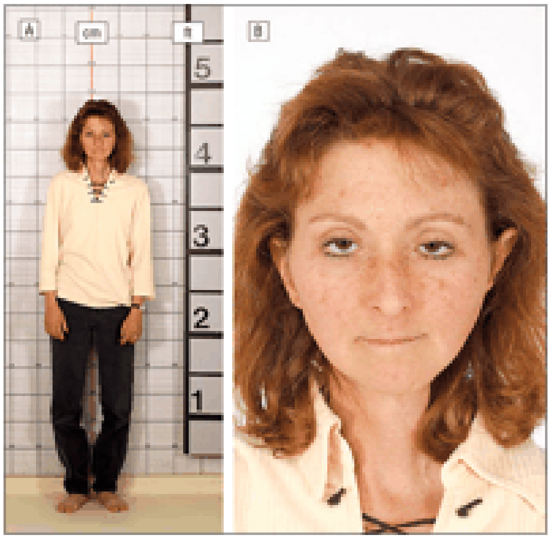
Inheritance :

Autosomal recessive with at least two loci and possibly multiple alleles

Clinical Synopsis

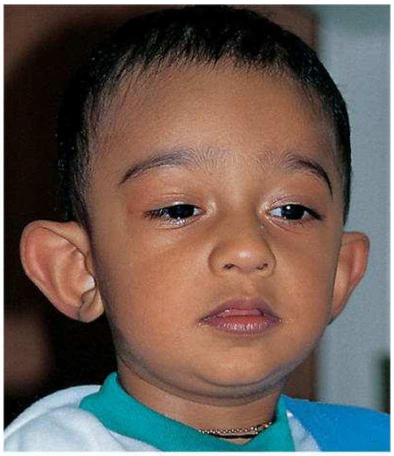
Gene map locus 16q24.3





Fragile X syndrome / OMIM 2008

Clinical Synopsis



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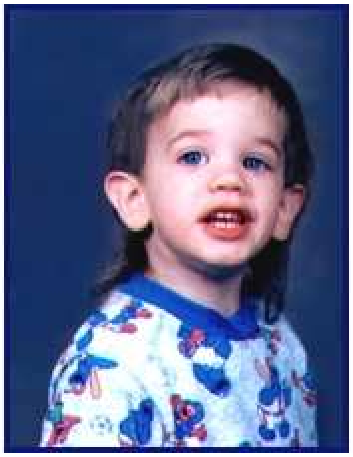

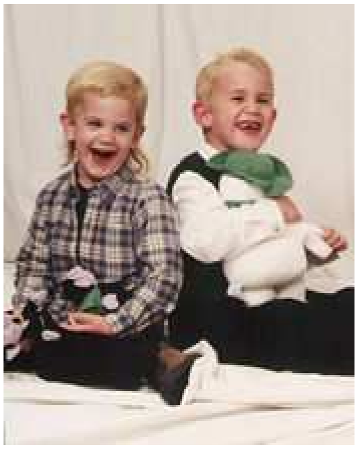

INHERITANCE :
    X-linked dominant

HEAD AND NECK :
    Head
    Macrocephaly
    Face
    Coarse facial features
    Large forehead
    Long face
    Prominent jaw
    Ears
    Large ears

CARDIOVASCULAR :
    Heart
    Mitral valve prolapse
    Cardiovascular
    Mild dilatation of ascending aorta

CHEST :
    Ribs, sternum, clavicles, and scapulae
    Pectus excavatum

GENITOURINARY :
    External genitalia, male
    Macroorchidism, postpubertal
    Congenital macroorchidism (some cases)

SKELETAL :
    Spine
    Scoliosis
    Limbs
    Joint laxity
    Feet
    Pes planus

NEUROLOGIC :
    Central nervous system
    Mental retardation (moderate to severe in males)
    Abnormal head movements

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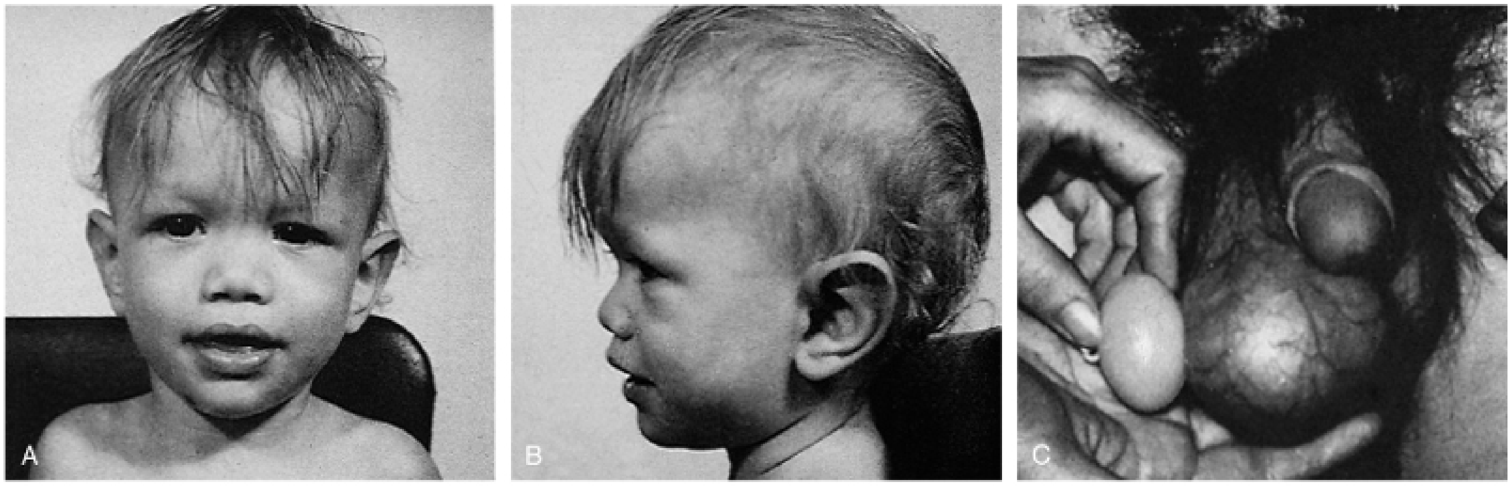
Behavioral/psychiatric manifestations
Hyperactive behavior
Poor eye contact
Autism

LABORATORY ABNORMALITIES :
Folate-dependent fragile site at Xq28

MISCELLANEOUS :
Incomplete penetrance
50% of females have learning disability or mild mental retardation
Prevalence approximately 1 in 4,000 males
Most cases (98%) caused by expanded trinucleotide repeat (CGG)n in the FMR1 gene
Repeat is unstable if > 52 repeats
Symptomatic if > 200 repeats

MOLECULAR BASIS

Caused by mutation in the FMR1 gene (309550.0004)



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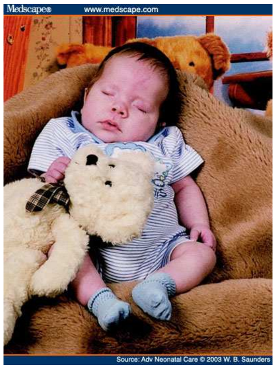
JOUBERT SYNDROME; JBTS / *OMIM 2008*
CEREBELLOOCULORENAL SYNDROME

Clinical Synopsis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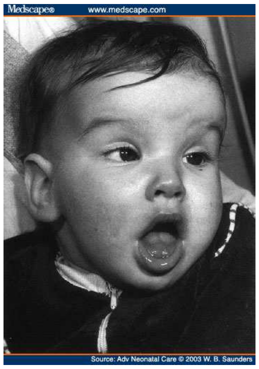
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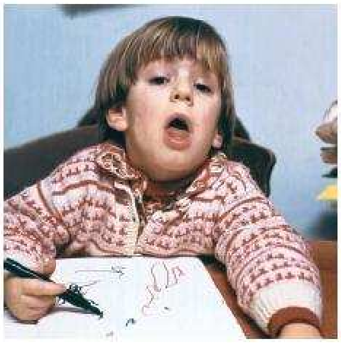
INHERITANCE :
- Autosomal recessive

HEAD AND NECK :
- **Head**
- Macrocephaly
- **Face**
- Prominent forehead
- High, rounded eyebrows
- Hemifacial spasms
- **Ears**
- Low-set ears
- 'Tilted' ears
- **Eyes**
- Abnormal, jerky eye movements
- Impaired smooth pursuit
- Impaired saccades

- Oculomotor apraxia
- Coloboma of optic nerve
- Chorioretinal coloboma
- Retinal dysplasia (less common)
- Retinal dystrophy (less common)
- Epicanthal folds
- Ptosis
- **Nose**
- Upturned nose



- Anteverted nostrils
- **Mouth**
- Triangular-shaped open mouth
- Protruding tongue
- Rhythmic tongue movements
- Soft tissue tumors of the tongue (less common)

RESPIRATORY :
- Neonatal breathing dysregulation

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Last update: 7 October 2008

Hyperpnea, episodic
Tachypnea, episodic
Central apnea

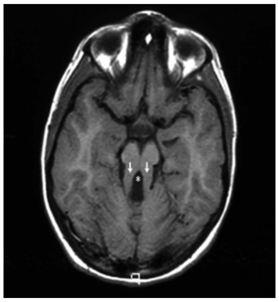
ABDOMEN :
Liver
Hepatic fibrosis (less common)

GENITOURINARY :
Kidneys
Renal cysts (less common)

SKELETAL :
Hands
Polydactyly, postaxial (less common)
Mussing digital phalanges (less common)
Feet
Polydactyly, postaxial (less common)

NEUROLOGIC :
Central nervous system
Delayed psychomotor development
Mental retardation
Ataxia
Hypotonia
Occipital meningocele (less common)
Occipital myelomeningocele (less common)
Hypoplasia of the brainstem
Malformation of brainstem structures
'Molar tooth sign' on MRI
Cerebellar vermis hypoplasia
Dysgenesis or agenesis of the cerebellar vermis
Deep posterior interpeduncular fossa
Thick and elongated superior cerebellar peduncles
Behavioral/psychiatric manifestations
Hyperactivity
Aggressiveness
Self-mutilation

MISCELLANEOUS :
Variable phenotype
Genetic heterogeneity (see JBTS2 608091, JBTS3 608629, JBTS4 609583)



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MARFAN SYNDROME; MFS / *OMIM 2008*

Clinical Synopsis

INHERITANCE :

Autosomal dominant

GROWTH :

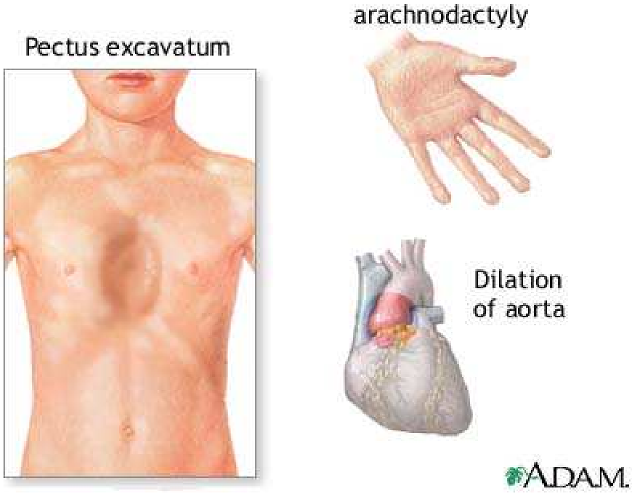
Height

Mean length at birth 53 +/- 4.4 cm for males
Mean length at birth 52.5 +/- 3.5 cm for females
Mean adult height 191.3 +/- 9 cm for males
Mean adult height 175.4 +/- 8.2 cm for females
Disproportionate tall stature, upper to lower segment ratio less than 0.85
Arm span to height > 1.05

Other

Puberty-associated peak in growth velocity is 2.4 years earlier for males and 2.2 years earlier for females

HEAD AND NECK :



Head

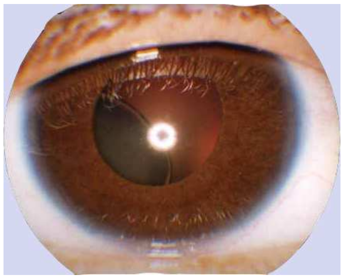
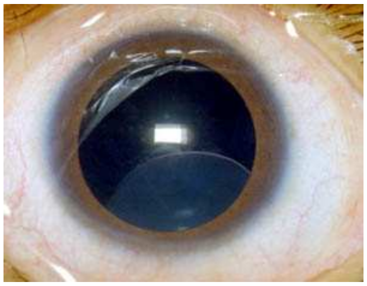
Dolichocephaly

Face

Long, narrow face
Malar hypoplasia
Micrognathia
Retrognathia

Eyes

Enophthalmos
Ectopia lentis
Myopia
Increased axial globe length
Corneal flatness
Retinal detachment
Iris hypoplasia
Early glaucoma
Early cataracts
Down-slanting palpebral fissures

Mouth

High-arched palate

Narrow palate
Teeth
Crowded teeth

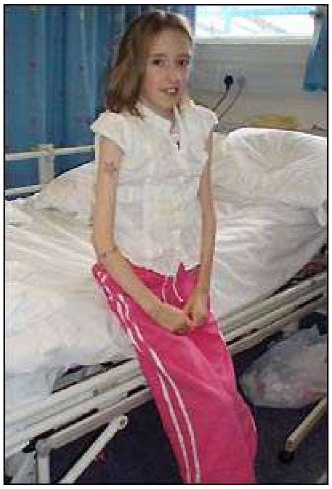
CARDIOVASCULAR :
Heart
Aortic regurgitation
Mitral regurgitation
Mitral valve prolapse
Congestive heart failure
Tricuspid valve prolapse
Premature calcification of mitral annulus
Vascular
Aortic root dilatation
Aortic dissection
Ascending aortic aneurysm
Aneurysm of other aortic segments rare
Pulmonary artery dilatation

RESPIRATORY :
Lung
Emphysema in most severe presentation
Pneumothorax
Pulmonary blebs

CHEST :
Ribs, sternum, clavicles, and scapulae
Pectus excavatum
Pectus carinatum
Pectus asymmetric sternum

ABDOMEN :
External features
Recurrent or incisional hernia

SKELETAL :
Premature arthritis
Spine
Scoliosis
Kyphoscoliosis
Thoracic lordosis
Spondylolisthesis
Lumbosacral dural ectasia
Pelvis
Protrusio acetabulae



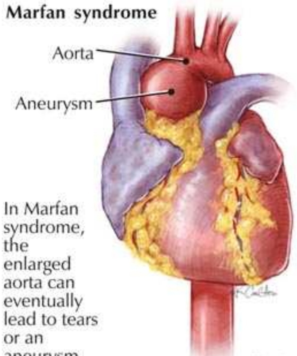
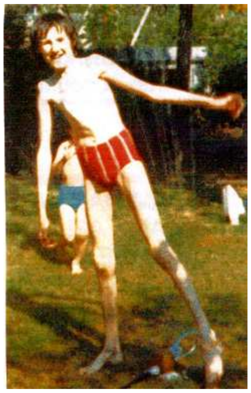

Marfan syndrome
Aorta
Aneurysm
In Marfan syndrome, the enlarged aorta can eventually lead to tears or an aneurysm.

Fig. 2



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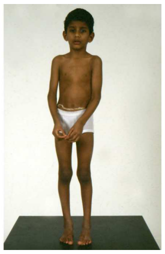
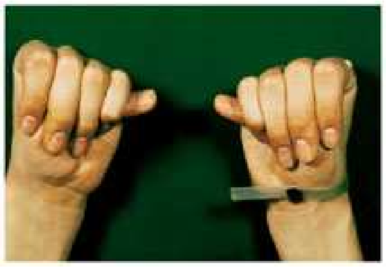
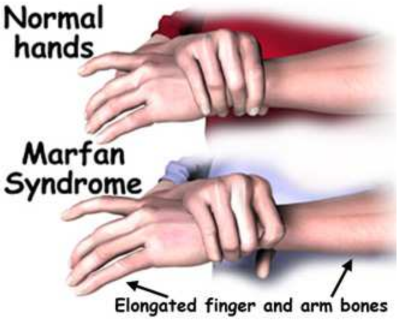
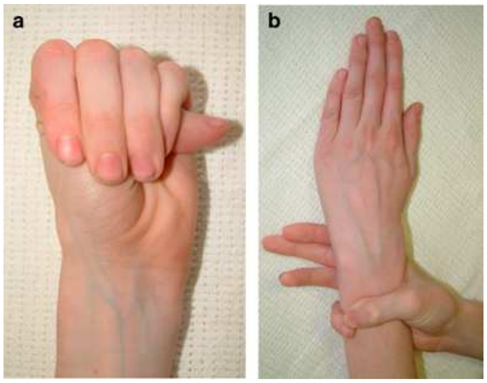




Limbs
Long bone overgrowth (dolichostenomelia)
Joint hypermobility
Joint contractures
Genu recurvatum
Hands
Arachnodactyly
Feet
Pes planus
Long, narrow feet
Pes cavus
Hammer toes
Medial rotation of the medial malleolus


Normal hands
Marfan Syndrome
Elongated finger and arm bones

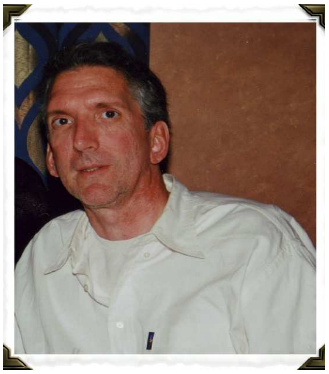
MUSCLE :
Decreased muscle mass
SKIN, NAILS, HAIR :
Skin
Striae distensae
Decreased subcutaneous fat

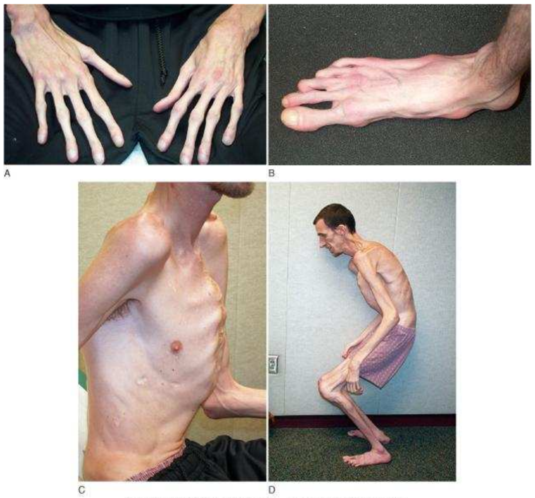


LABORATORY ABNORMALITIES :
Decreased fibrillin-1 immunostaining in the dermis
MISCELLANEOUS :
About 25% of cases due to new mutations

MOLECULAR BASIS

Caused by mutations in the fibrillin-1 gene (FBN1, 134797.0001)





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NEUROFIBROMATOSIS, TYPE I; NF1 / *OMIM2008*
VON RECKLINGHAUSEN DISEASE

Clinical Synopsis

INHERITANCE :

Autosomal dominant

HEAD AND NECK :

Head

Macrocephaly , Sphenoid dysplasia

Eyes

Lisch nodules (iris hamartomas)

Glaucoma

Hypertelorism

CARDIOVASCULAR :

Vascular

Renal artery stenosis

Hypertension

SKELETAL :

Spine

Scoliosis

Spina bifida

Limbs

Pseudoarthrosis

Thinning of long bone cortex

Local bony overgrowth

SKIN, NAILS, HAIR :

Skin

Neurofibromas

Plexiform neurofibroma

Cafe-au-lait spots

Axillary freckling

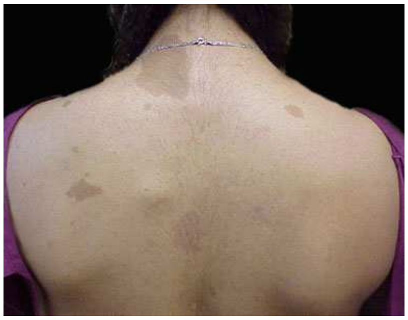
Inguinal freckling

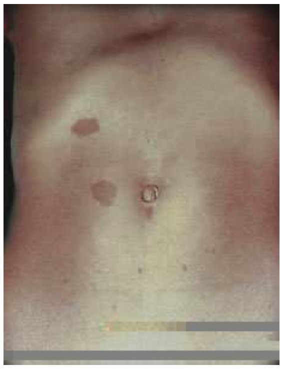
NEUROLOGIC :

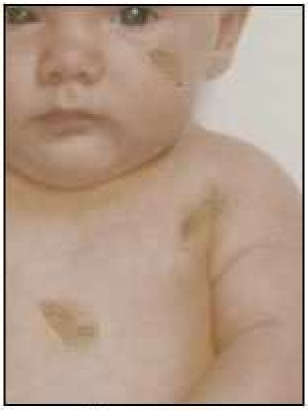
Central nervous system

Mental retardation, 30% learning disabilities, 10% mild mental retardation

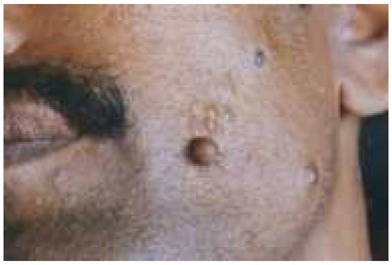
Aqueductal stenosis

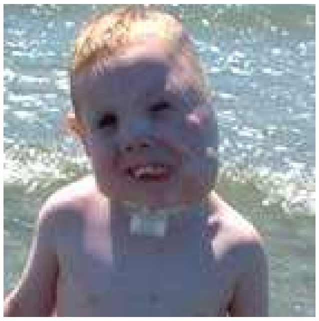


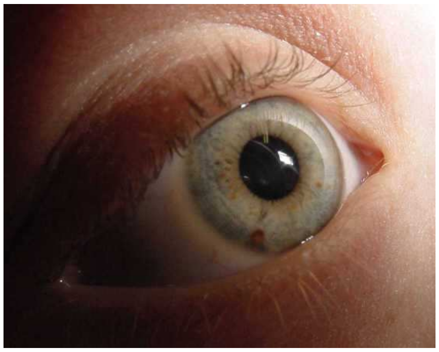




café-au-lait spots







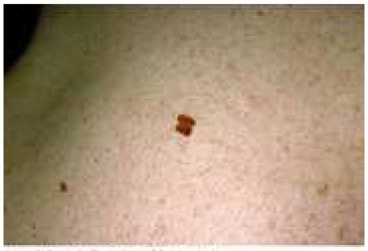
Welcome to feedback and comment on email: mostafaelbaba@hotmail.com
Last update: 7 November 2008

Hydrocephalus

NEOPLASIA :

Optic glioma
Meningioma
Hypothalamic tumor
Neurofibrosarcoma
Rhabdomyosarcoma
Duodenal carcinoid
Somatostatinoma
Parathyroid adenoma
Pheochromocytoma
Pilocytic astrocytoma
Malignant peripheral nerve sheath tumors

Tumors at multiple other sites including CNS



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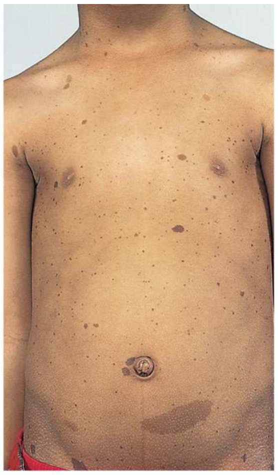

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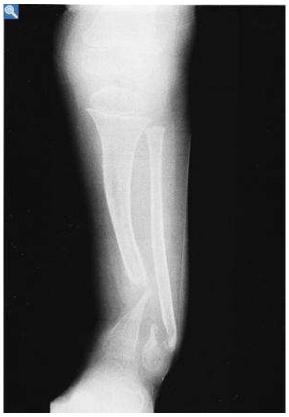
MISCELLANEOUS :

50% of cases are caused by new mutations

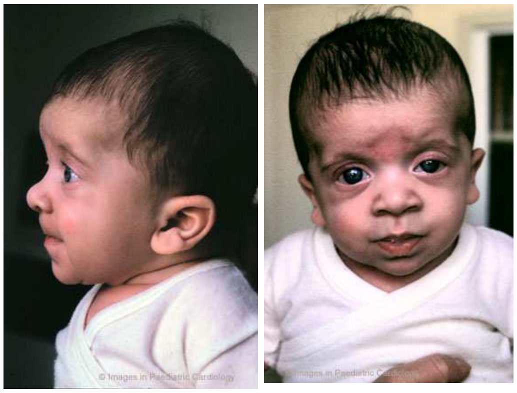
MOLECULAR BASIS :

- Gene map locus 17q11.2
- Caused by mutations in the neurofibromin gene (NF1, 162200.0001)



NOONAN SYNDROME 1; NS1/ *OMIM 2008*

Clinical Synopsis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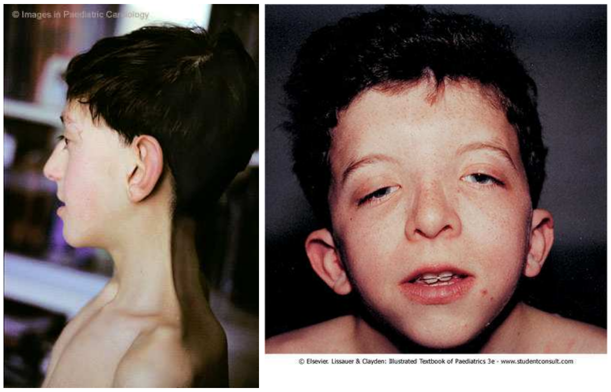
INHERITANCE :
Autosomal dominant
GROWTH :
Height
Short stature (postnatal onset)
Other
Failure to thrive in infancy
Specific growth curves are available
HEAD AND NECK :
Face
Triangular face with age
Ears
Low-set posteriorly rotated ears
Nerve deafness
Eyes
Ptosis
Hypertelorism
Down-slanting palpebral fissures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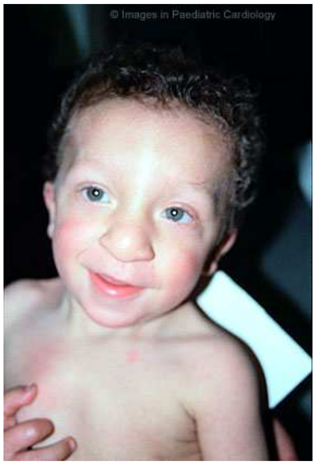
Epicanthal folds
Myopia
Blue-green irides
Mouth
Deeply grooved philtrum
High peaks of upper lip
vermilion border
High arched palate
Micrognathia
Dental malocclusion
Neck
Low posterior hairline
Webbed neck
Cystic hygroma
CARDIOVASCULAR :
Heart
Congenital heart defect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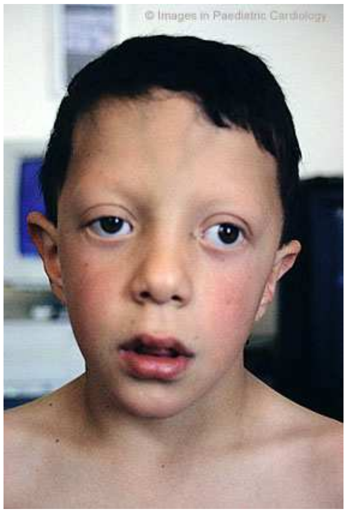
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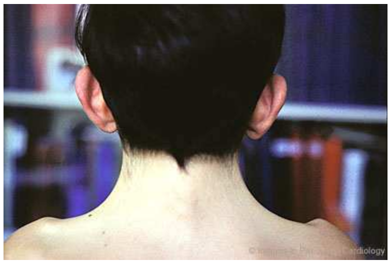
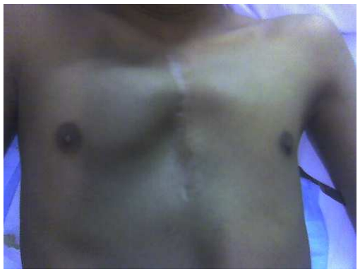
Atrial septal defects
Ventricular septal defects
Pulmonic stenosis
Vascular
Patent ductus arteriosus

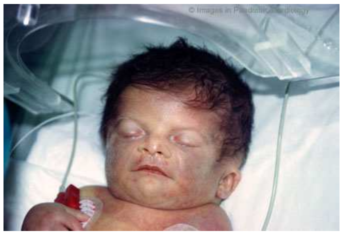


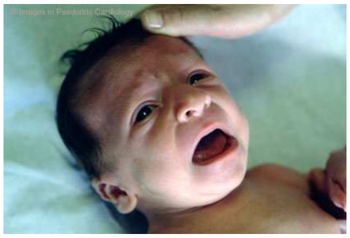
CHEST :
Ribs, sternum, clavicles, and scapulae
Shield chest
Pectus carinatum superiorly
Pectus excavatum inferiorly



GENITOURINARY :
Internal genitalia, male
Occasional hypogonadism
Cryptorchidism
Male infertility in individuals with bilateral cryptorchidism

SKELETAL :
Spine
Vertebral abnormalities
Limbs
Cubitus valgus
Clinodactyly
Brachydactyly
Blunt fingertips

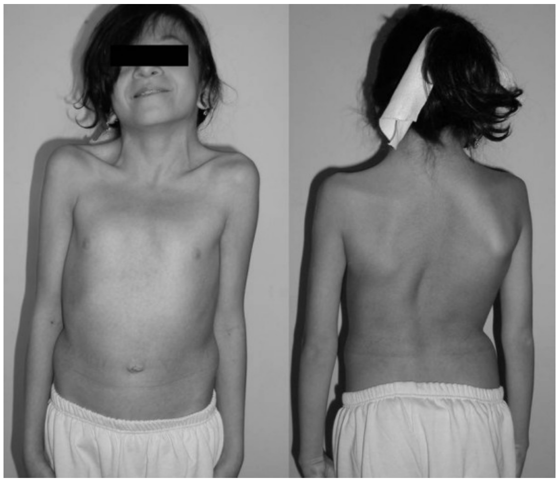




SKIN, NAILS, HAIR :
Hair
Wooly-like consistency of hair

MUSCLE, SOFT TISSUE :
Lymphedema

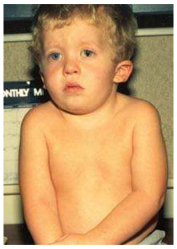
NEUROLOGIC :
Central nervous system
Articulation difficulties
Mental retardation (25%)



HEMATOLOGY :
Amegakaryocytic thrombocytopenia
Von Willebrand disease
Bleeding tendency

NEOPLASIA :
Malignant schwannoma

LABORATORY ABNORMALITIES :
Partial deficiency of factor XI:C



Partial deficiency of factor XII:C
Partial deficiency of factor XIII:C
Thrombocytopenia

MISCELLANEOUS :

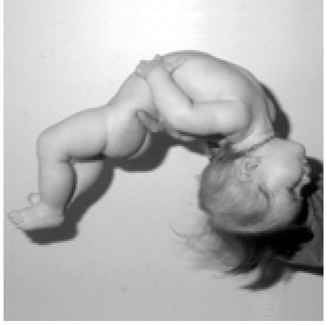
Genetic heterogeneity (see NS2 605275 and NS3 609942)
Allelic with LEOPARD syndrome (151100)

MOLECULAR BASIS

Caused by mutations in the protein tyrosine phosphatase, nonreceptor-type, 11 gene (PTPN11, 176876.0001)

PRADER-WILLI SYNDROME; PWS / *OMIM2008*

Clinical Synopsis



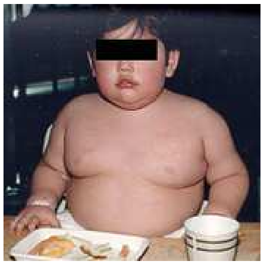
INHERITANCE :

Isolated cases

GROWTH :

Height

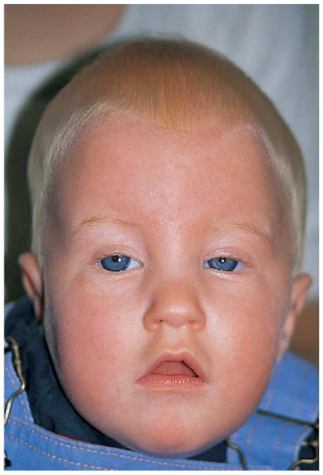
Normal birth length
Length deceleration in first few months
Mean adult male height, 155 cm
Mean adult female height, 147 cm
Steady childhood growth
Fall-off in adolescent growth



Weight

Failure to thrive in infancy
Onset of obesity from 6 months to 6 years
Central obesity

HEAD AND NECK :



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Head

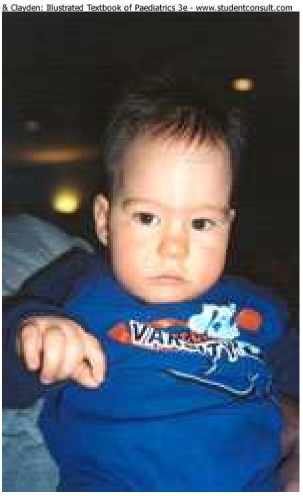
Dolichocephaly

Face

Narrow bitemporal diameter

Eyes

Almond-shaped eyes
Strabismus
Upslanting palpebral fissures
Myopia
Hyperopia



Mouth

Thin upper lip
Small-appearing mouth
Down-turned corners of mouth
Thick, viscous saliva

Teeth

Early dental caries

RESPIRATORY :

Hypoventilation
Hypoxia

ABDOMEN :

Gastrointestinal
Feeding problems in infancy requiring gavage feeds
Decreased vomiting

GENITOURINARY :

External genitalia, male
Hypogonadotropic hypogonadism
Small penis
Scrotal hypoplasia

External genitalia, female
Hypoplastic labia minora
Hypoplastic clitoris

Internal genitalia, male
Cryptorchidism

Internal genitalia, female
Amenorrhea
Oligomenorrhea

SKELETAL :

Osteoporosis
Osteopenia

Spine
Scoliosis
Kyphosis

Hands
Small hands (<25th percentile for height age)
Narrow hands with straight ulnar border
Clinodactyly
Syndactyly

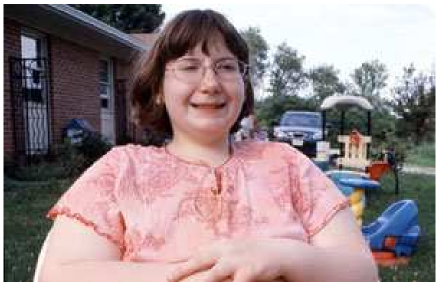
Feet
Small feet (<10th percentile for height age)

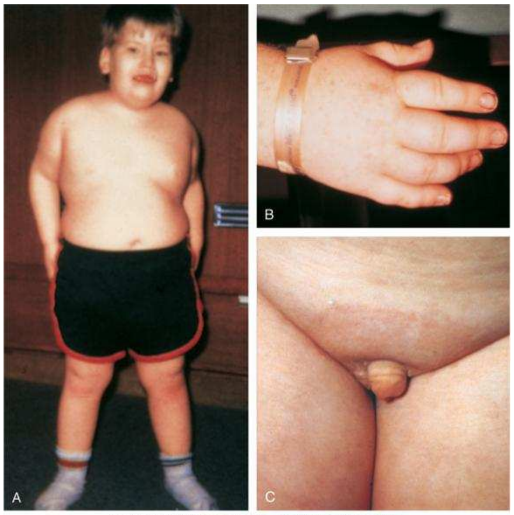
SKIN, NAILS, HAIR :

Hypopigmentation

Skin
Fair skin
Sun sensitivity

Hair
Blonde to light brown hair
Frontal hair upsweep





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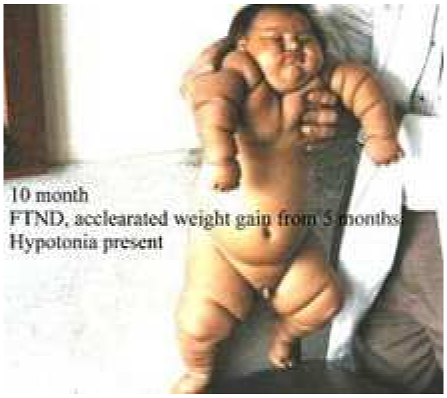
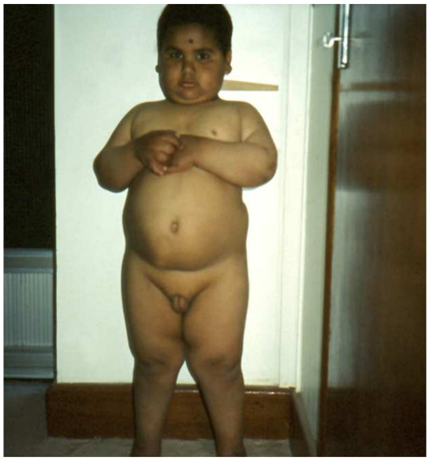
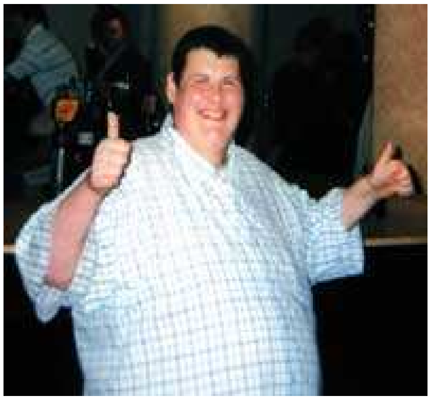


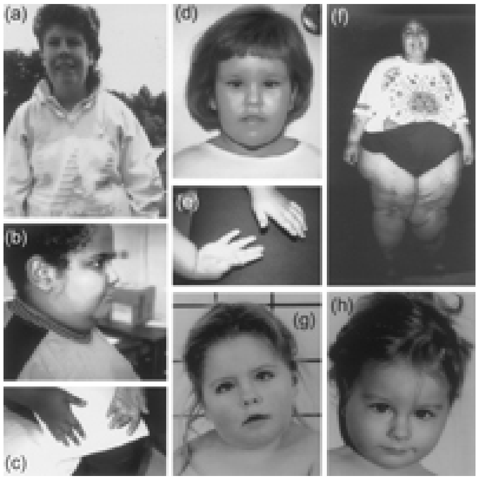




NEUROLOGIC :

Central nervous system

- Mild-to-moderate mental retardation (~90%)
- Learning disabilities
- Severe neonatal hypotonia improving with age
- Normal neuromuscular studies
- Seizures
- Poor gross motor coordination
- Poor fine motor coordination
- Global developmental delay
- Behavioral problems
- Sleep disturbances
- High pain threshold
- Poor neonatal suck and swallow reflexes
- Speech articulation problems
- Childhood polyphagia



VOICE :

- Hypernasal speech
- Weak or squeaky cry in infancy

ENDOCRINE FEATURES :

- Hyperinsulinemia
- Growth hormone deficiency
- Hypogonadotropic hypogonadism

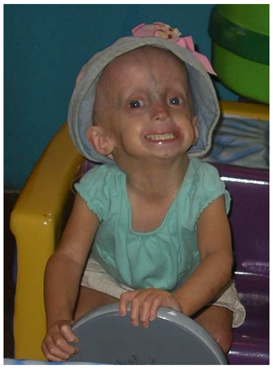
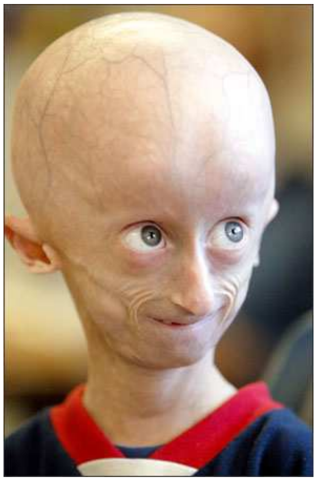
MISCELLANEOUS :

- Excessive skin picking of sores
- Food related behavioral problems include excessive appetite and obsession with eating
- Temperature instability
- High pain threshold
- Decreased fetal activity
- Breech position
- Behavioral problems including stubbornness and rage
- Sleep disturbance or sleep apnea (obstructive, central, or mixed)
- Unusual skill with jigsaw puzzle

MOLECULAR BASIS

- Microdeletion of 15q11 in 70% of patients confirmed by fluorescent in situ hybridization
- Remainder of cases secondary to maternal disomy
- Rare cases secondary to chromosome translocation

HUTCHINSON-GILFORD PROGERIA SYNDROME; HGPS / *OMIM2008*

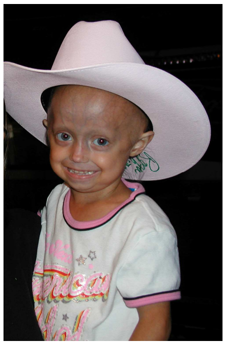
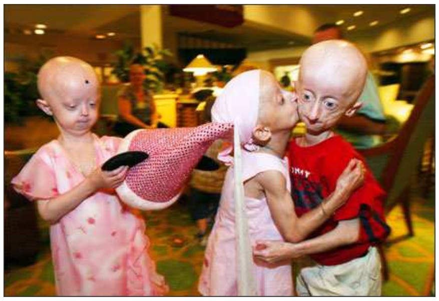
Clinical Synopsis

INHERITANCE :
Autosomal dominant

GROWTH :
Other
Postnatal onset growth retardation

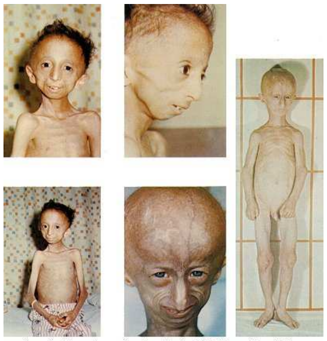
HEAD AND NECK :
Face

Midface hypoplasia
Micrognathia

CARDIOVASCULAR :
Cardiac
Premature atherosclerosis
Premature coronary artery disease
Angina pectoris
Myocardial infarction
Congestive heart failure

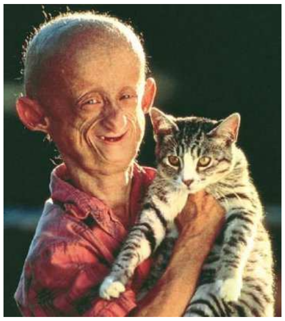
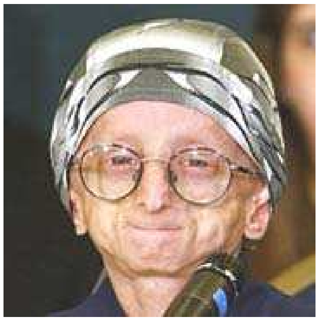
SKELETAL :
Generalized osteoporosis with pathologic fractures



Progeria: Premature aging. Usually die at 10-15 yrs.of heart failure.
SS Gellis, M Feingold. Atlas of Mental Retardation Syndromes. 1968.

SKIN, NAILS, HAIR :
Skin: Absence of subcutaneous fat
Hair: Alopecia

MISCELLANEOUS :
Probably autosomal dominant with rare instances of affected sibs due to germinal mosaicism
Premature aging
Median life expectancy, 13.4 years
Paternal age effect

MOLECULAR BASIS

Gene map locus 1q21.2
Caused by mutation in the lamin A/C gene (LMNA, 150330.0022)

RETT SYNDROME; RTT / *OMIM2008*

Clinical Synopsis

INHERITANCE :

X-linked dominant

GROWTH :

Height

Short stature

Weight

Cachexia

HEAD AND NECK :

Head

Normal birth head circumference
Deceleration of head growth
Microcephaly

Teeth

Bruxism

CARDIOVASCULAR :

Heart

Prolonged QTc interval

T-wave abnormalities

RESPIRATORY :

Periodic apnea while awake
Intermittent hyperventilation
Breath holding

ABDOMEN :

Gastrointestinal

Constipation
Gastroesophageal reflux

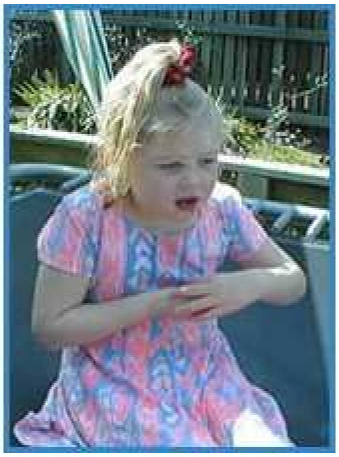
SKELETAL :

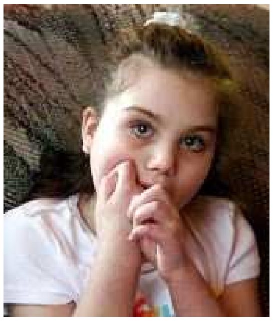
Spine

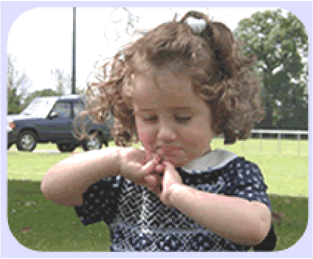
Scoliosis
Kyphosis

Feet

Small feet
Cold feet
Vasomotor disturbance







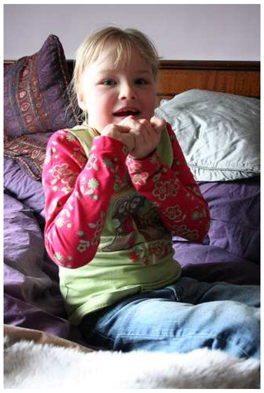
MUSCLE :

Muscle wasting

NEUROLOGIC :

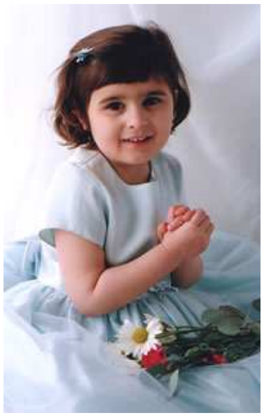
Central nervous system

Normal development until 6-18 months
Mental retardation, profound
Spasticity
EEG abnormalities - slow waking background, intermittent rhythmical slowing (3-5Hz), epileptiform discharges
Seizures
Reduction or loss of acquired skills (e.g., purposeful hand use, speech)
Gait ataxia
Gait apraxia
Truncal ataxia
Dystonia
Cortical atrophy (frontal area)



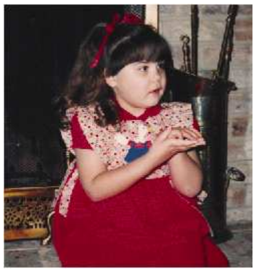
Behavioral/psychiatric manifestations

Autistic behaviors
Hand stereotypies (e.g., hand wringing)
Sleep disturbance
Bruxism
Breath holding



MISCELLANEOUS :

Prevalence 1/10,000-1/15,000 female births
Initially normal for first 6-18 months which is then followed by withdrawal and regression
Four clinical stages - Stage I, early onset stagnation (onset 6 months-1.5 year)
Stage II, rapid developmental regression (onset 1-4 years)
Stage III, pseudostationary period (onset 2-10 years)
Stage IV, late motor deterioration (when ambulation ceases)
Most cases are sporadic
De novo mutations occur almost exclusively on the paternally derived X chromosome

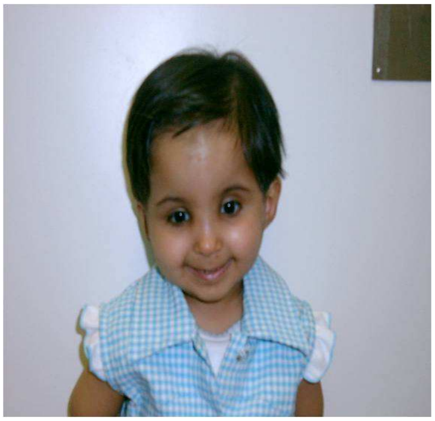


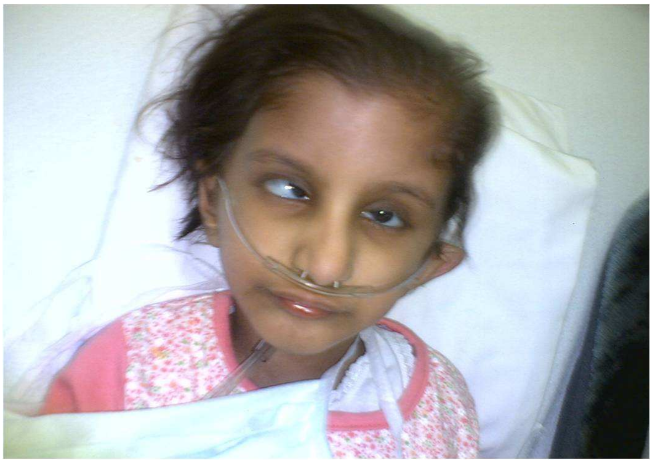
MOLECULAR BASIS

Caused by mutations in the methyl-CpG-binding protein-2 gene (MECP2, 300005.0001)

SANJAD-SAKATI SYNDROME/ *OMIM 2008* HYPOPARATHYROIDISM-RETARDATION-DYSMORPHISM SYNDROME; HRD

Clinical Synopsis





INHERITANCE :

Autosomal recessive

GROWTH :

Other

Severe intrauterine growth retardation
Postnatal growth retardation

HEAD AND NECK :

Head

Microcephaly

Face

Micrognathia
Prominent forehead
Long philtrum

Ears

Low-set ears
Posteriorly rotated ears

Eyes

Deep-set eyes

Nose

Beaked nose
Depressed nasal bridge

Mouth

Thin lips
Bifid uvula

GENITOURINARY :

External genitalia, male

Micropenis

Internal genitalia, male

Cryptorchidism

SKELETAL :

Delayed bone age
Patchy osteosclerosis

Hands

Small hands

Feet

Small feet

NEUROLOGIC :

Central nervous system

Tetany
Hypocalcemic seizures
Mental retardation
Mild-moderate ventricular dilatation

ENDOCRINE FEATURES :

Low parathyroid hormone
Congenital hypoparathyroidism

IMMUNOLOGY :

Normal cell mediated immunity
Recurrent bacterial infections

LABORATORY ABNORMALITIES :

Hypocalcemia
Hyperphosphatemia

MISCELLANEOUS :

Allelic with Kenny-Caffey syndrome type 2 (244460)

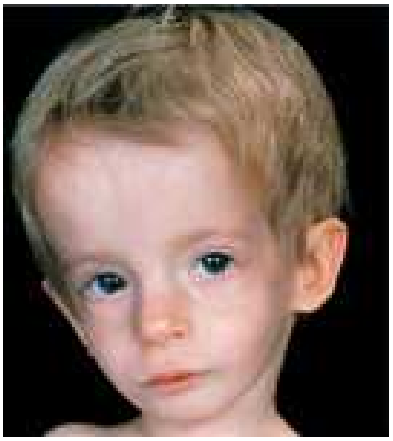
MOLECULAR BASIS

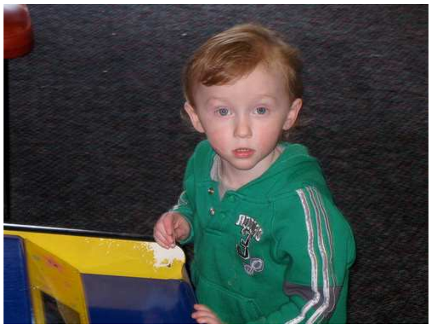
Caused by mutation in the tubulin-specific chaperone E gene (TCBE, 604934.0001)

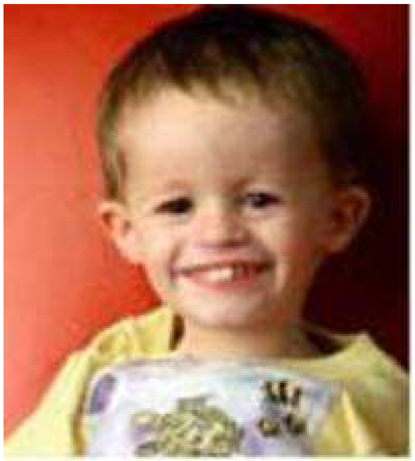
Gene map locus 1q42-q43

SILVER-RUSSELL SYNDROME; SRS

Clinical Synopsis







INHERITANCE :

Isolated cases

GROWTH :

Height

Average adult male height, 149.5 cm

Average female adult height, 138 cm

Weight

Small for gestational age infant

Other

Lateral asymmetry

Partial or total asymmetry

Intrauterine growth retardation

HEAD AND NECK :

Head

Pseudohydrocephalic appearance

Normal head circumference

Face

Small, triangular facies

Micrognathia

Frontal bossing

Eyes

Blue sclera in infancy

Mouth

Down turned corners of mouth

CARDIOVASCULAR :

Heart

Cardiac defects

GENITOURINARY :

Ureters

Posterior urethral valves

Hypospadias

SKELETAL :

Skeletal maturation retardation

Skull

Craniofacial disproportion

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Last update: 4 October 2008

Delayed fontanel closure

Limbs

Asymmetry of arms and/or legs

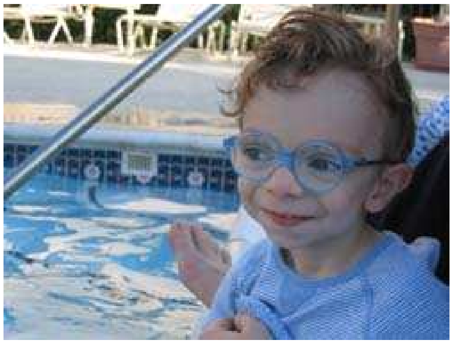
Hands

Fifth finger clinodactyly

Fifth digit middle or distal phalangeal hypoplasia

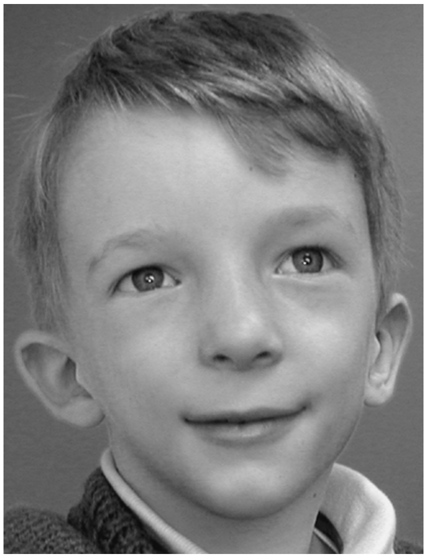
Feet

Syndactyly of 2nd-3rd toes



SKIN, NAILS, HAIR :

Cafe-au-lait spots



NEUROLOGIC :

Central nervous system

Developmental delay

ENDOCRINE FEATURES :

Fasting hypoglycemia

Growth hormone deficiency in some individuals

NEOPLASIA :

Craniopharyngioma

Testicular seminoma

Wilms tumor

Hepatocellular carcinoma

MISCELLANEOUS :

Marked heterogeneity

Majority cases are sporadic

Chromosome rearrangements gave been reported

Maternal uniparental disomy (UPD)7 reported in some cases

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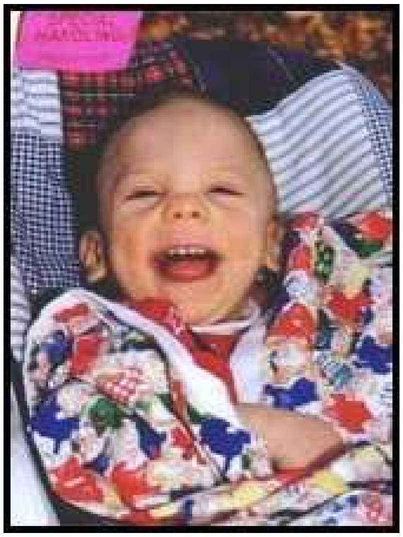
Last update: 4 October 2008

SMITH-LEMLI-OPITZ SYNDROME; SLOS / *OMIM 2008*

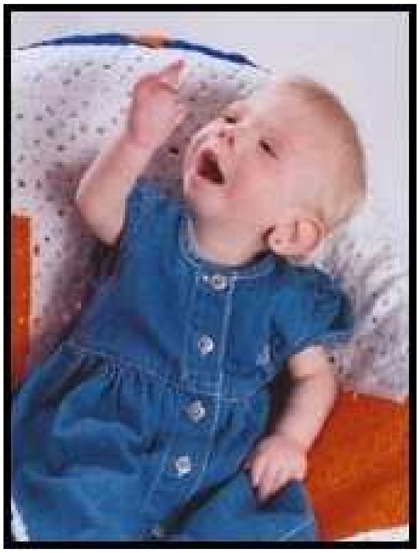
Clinical Synopsis



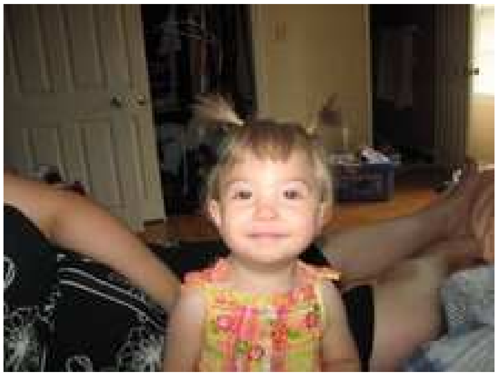
INHERITANCE :
Autosomal recessive

GROWTH :
Height
Short stature
Weight
Birth weight <2500gm
Other
Failure to thrive

HEAD AND NECK :
Head
Microcephaly
Face
Micrognathia
Bitemporal narrowing
Ears
Low-set ears
Posteriorly rotated ears

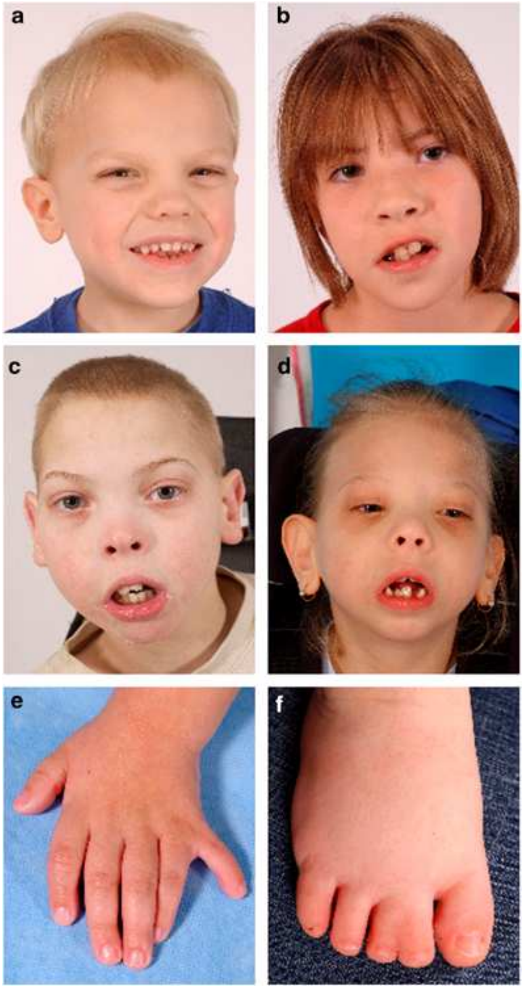


Eyes
Ptosis
Epicanthal folds
Cataracts
Hypertelorism
Strabismus
Nose
Anteverted nares
Broad, flat nasal bridge
Mouth
Cleft palate
Hypoplastic tongue
Broad alveolar margins



Teeth
Large central front teeth
Dental crowding

CARDIOVASCULAR :
Heart
Ventricular septal defect
Atrial septal defect



Vascular
Coarctation of aorta
Patent ductus arteriosus

RESPIRATORY :

Lung
Hypoplastic lungs
Incomplete lobulation of the lungs

ABDOMEN :

Gastrointestinal
Poor suck
Vomiting
Constipation
Malrotation
Pyloric stenosis

GENITOURINARY :

External genitalia, male
Hypospadias
Ambiguous genitalia
Micropenis
Hypoplastic scrotum
Bifid scrotum
Microurethra

Internal genitalia, male
Cryptorchidism

Kidneys
Renal agenesis
Hydronephrosis
Single kidney
Cystic kidneys

Ureters
Ureteropelvic junction obstruction

SKELETAL :

Stippled epiphyses

Pelvis
Hip dislocation
Hip subluxation

Limbs
Limb shortening

Hands
Short thumbs
Postaxial polydactyly
Proximally placed thumbs

Feet

Syndactyly of second and third toes
Postaxial polydactyly
Talipes calcaneovalgus
Short, broad toes
Overriding toes
Metatarsus adductus

SKIN, NAILS, HAIR :
Skin
Severe photosensitivity
Eczema
Facial capillary hemangioma
Hair
Blonde hair

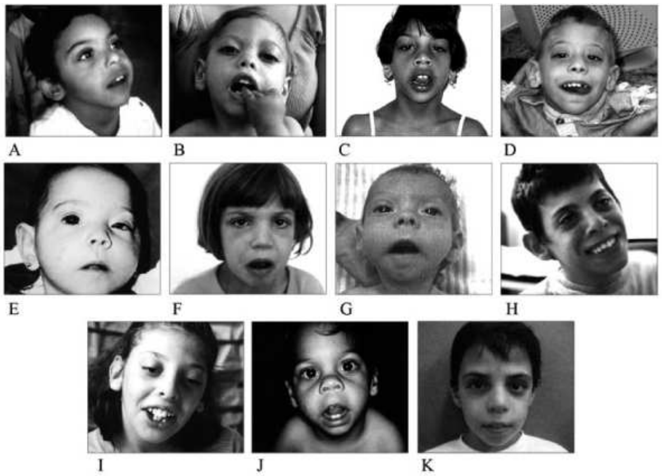
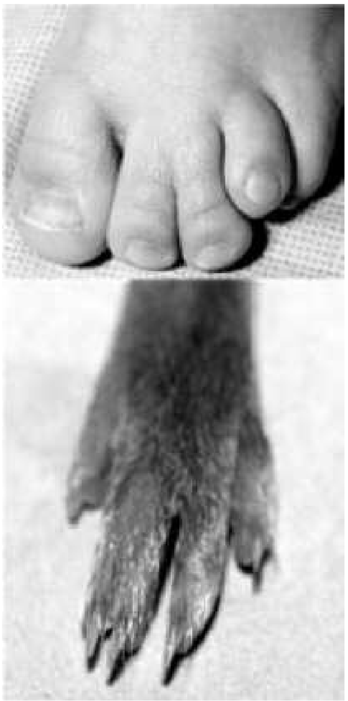


Figure 1 - Facial appearance of our confirmed cases of Smith-Lemli-Opitz syndrome (SLOS): (A) patient 1, (B) patient 2, (C) patient 3, (D) patient 4, (E) patient 5, (F) patient 6, (G) patient 7, (H) patient 8, (I) patient 9, (J) patient 10, (K) patient 11.

NEUROLOGIC :
Central nervous system
Mental retardation
Seizures
Hypotonia (early infancy)
Hypertonia (childhood)
Hydrocephalus
Frontal lobe hypoplasia
Periventricular gray matter heterotopias
Abnormal sleep pattern
Behavioral/psychiatric manifestations
Self injurious behavior
Aggressive behavior



VOICE :
Shrill screaming

PRENATAL MANIFESTATIONS :
Movement
Decreased fetal movement
Delivery
Breech presentation

LABORATORY ABNORMALITIES :
Low cholesterol
Elevated 7-dehydrocholesterol

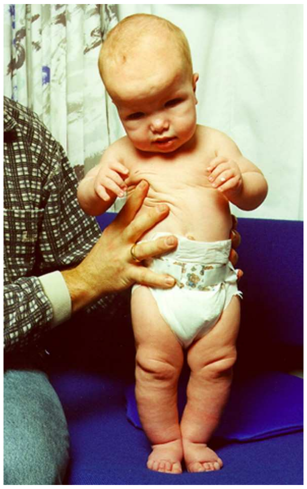
MISCELLANEOUS :
Estimated incidence 1/20,000 - 1/40,000

MOLECULAR BASIS

- Caused by mutations in the delta-7-dehydrocholesterol reductase gene (DHCR7, 602858.0001)
- Gene map locus 11q12-q13

SOTOS SYNDROME / CEREBRAL GIGANTISM / *OMIM2008*

Clinical Synopsis



GROWTH :

Height

Mean full term birth length 55.2cm

Length at or greater than 97th percentile through early adolescence

Adult height often normal

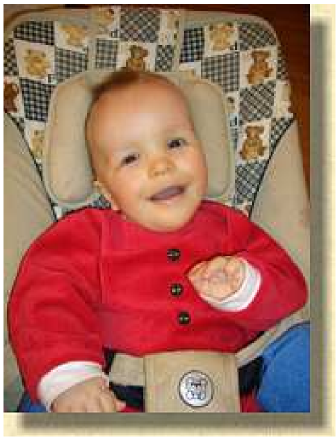
Mean male adult height 184.3cm

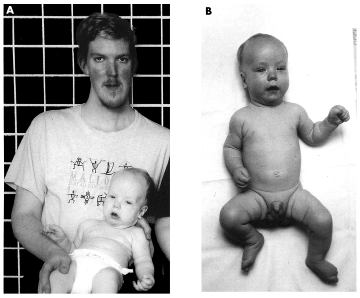
Mean female adult height 172.9cm

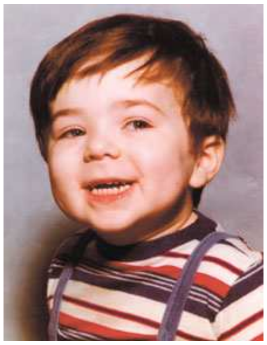
Weight

Mean full term birth weight 3.9kg

Birth length often more increased than weight







HEAD AND NECK :

Head

Macrocephaly

Dolichocephaly

Face

Frontal bossing

Prognathism

Pointed chin

Ears

Otitis media

Conductive hearing loss

Eyes

Downslanting palpebral fissures

Nystagmus

Strabismus

Hyperopia

Mouth

High arched palate

Teeth

Premature tooth eruption

CARDIOVASCULAR :

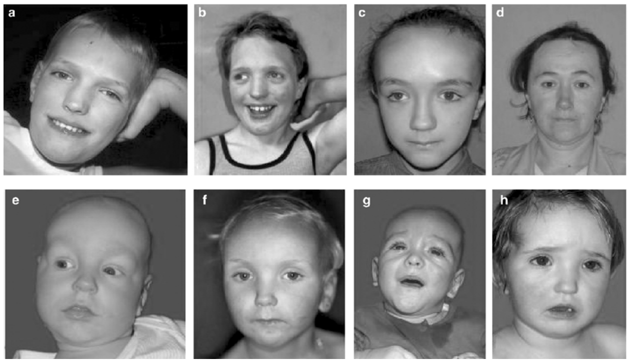
Heart

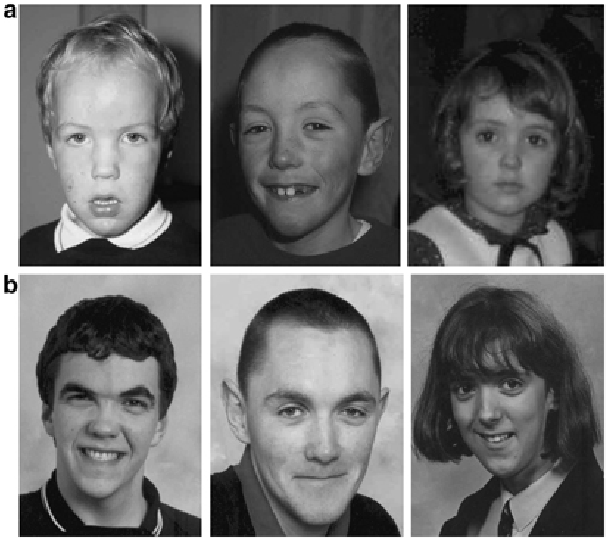
Atrial septal defect

Ventricular septal defect

Vascular

Patent ductus arteriosus





SKELETAL :

Advanced bone age

Limbs

Joint laxity

Genu valgus

Long arm span

Hands

Large hands

Disharmonic maturation of phalanges and carpal bones

Feet

Pes planus, Large feet

SKIN, NAILS, HAIR :

Nails

Thin brittle fingernails

Hair

Sparse hair in frontoparietal area

NEUROLOGIC :

Central nervous system

Developmental delay

Variable mental retardation

Neonatal hypotonia

Hyperreflexia

Poor coordination

Seizures

Behavioral problems

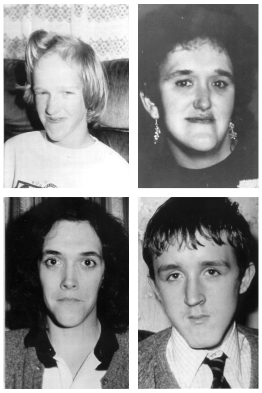
Expressive language delay

Partial to complete agenesis of corpus callosum

Persistent cavum septum pellucidum

Large cisterna magna

Ventriculomegaly , Prominent trigone and occipital horns



MISCELLANEOUS :

Majority of cases are sporadic . Few familial (parent offspring) cases reported

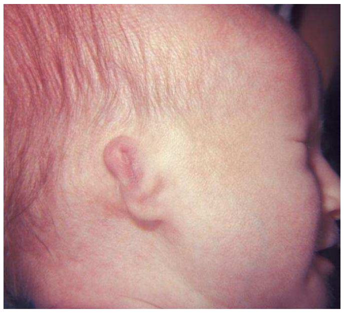
Slight increased risk for malignancy; Wilms tumor

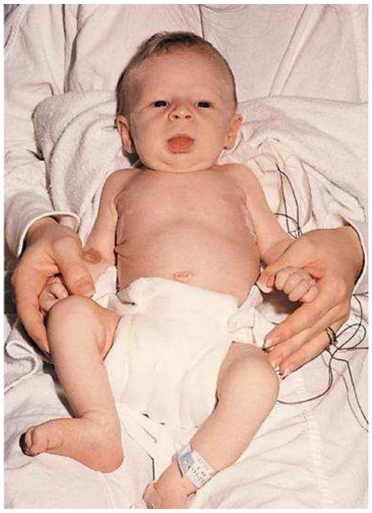
MOLECULAR BASIS

- Gene map locus 5q35
- Mutation in the nuclear receptor binding SET domain protein 1 gene (NSD1, 606681.0001)

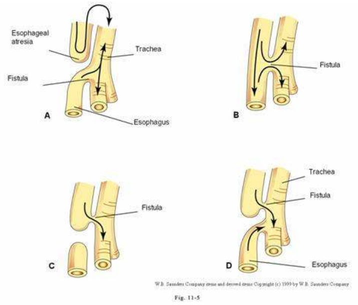
VATER (VACTERL) association / *OMIM 2008*

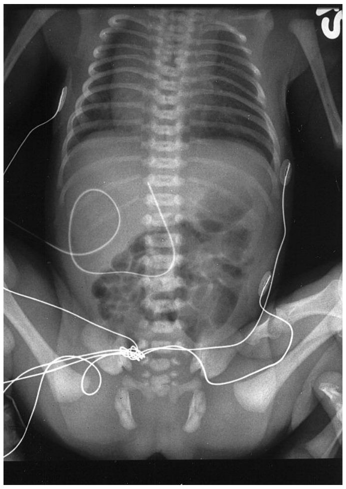
Clinical Synopsis

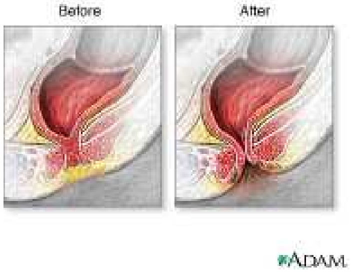


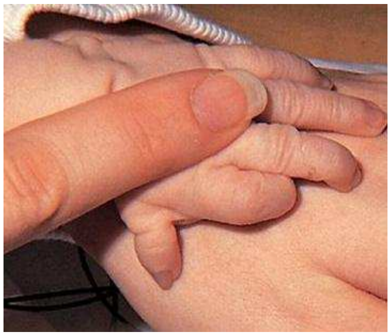


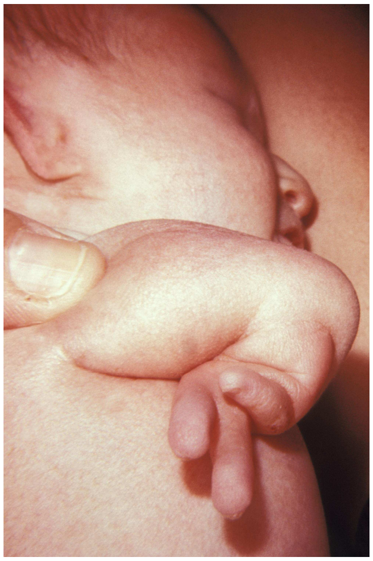
INHERITANCE :
    Isolated cases
GROWTH :
    Weight
    Failure to thrive
    Other
    Prenatal growth deficiency
    Postnatal growth deficiency
HEAD AND NECK :
    Head
    Large fontanels
CARDIOVASCULAR :
    Heart
    Ventricular septal defects
    Tetralogy of Fallot
    Transposition of the great arteries
    Vascular
    Patent ductus arteriosus
RESPIRATORY :
    Nasopharynx
    Choanal atresia
    Larynx
    Laryngeal stenosis
    Airways
    Tracheal agenesis
CHEST :
    Ribs, sternum, clavicles, and scapulae
    Rib anomalies
    Sternal anomalies
ABDOMEN :
    Gastrointestinal
    Tracheoesophageal fistula
    Esophageal atresia
    Anal atresia
GENITOURINARY :
    External genitalia, male


Esophageal atresia
Trachea
Fistula
A
Esophagus
B
Fistula
C
Fistula
D
Trachea
Fistula
Esophagus
Fig. 11-5

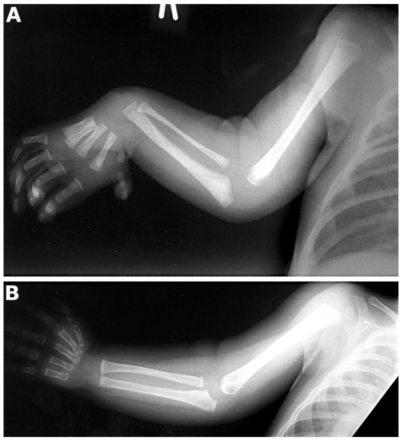



Before
After
ADAM





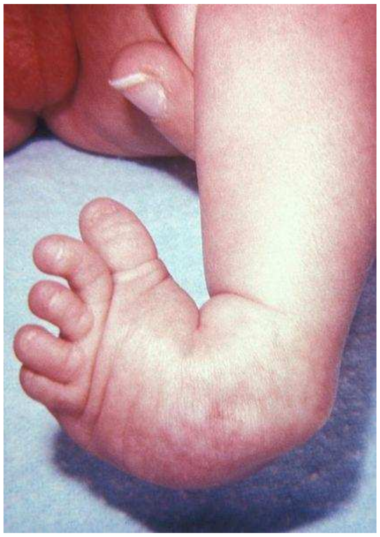
Hypospadias
Kidneys
Renal aplasia
Renal dysplasia
Hydronephrosis
Renal ectopia
Ureters
Vesicoureteral reflux



Ureteropelvic junction obstruction
Bladder
Persistent urachus

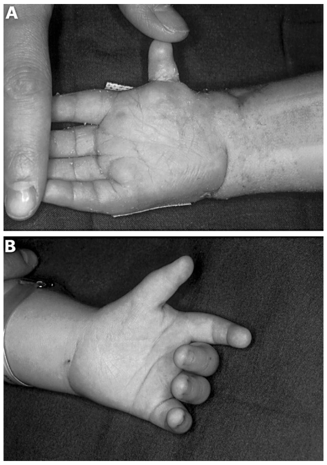
SKELETAL :

Spine
Vertebral anomalies
Scoliosis
Limbs
Radial aplasia
Radial hypoplasia
Radioulnar synostosis
Hands
Thumb hypoplasia
Preaxial polydactyly
Syndactyly
Triphalangeal thumb



NEUROLOGIC :

Central nervous system
Tethered cord
Spinal dysrhaphia
Occipital encephalocele

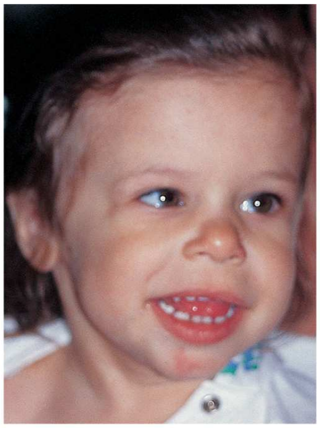


MISCELLANEOUS :

Single umbilical artery
Seen more frequently in infants of diabetic mothers
Estimated frequency 1.6 cases/10,000 live births
Nonrandom association of following anomalies--V (vertebral anomalies), A (anal atresia), C (cardiovascular anomalies), T (tracheoesophageal fistula), E (esophageal atresia), R (renal anomalies), L (preaxial limb anomalies)
Diagnosis made if 3/7 defects are present

WILLIAMS-BEUREN SYNDROME; WBS/ *OMIM 2008*
WILLIAMS SYNDROME

Clinical Synopsis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INHERITANCE :

Autosomal dominant

GROWTH :

Short stature

Other

Intrauterine growth retardation

HEAD AND NECK :

Face

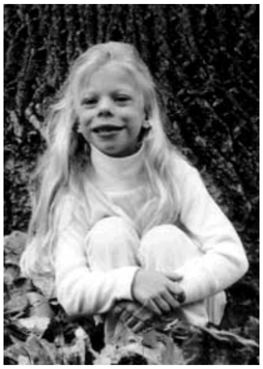
Medial eyebrow flare

Flat midface

Periorbital fullness (puffy eyes)

Epicanthal folds

Long philtrum



Ears

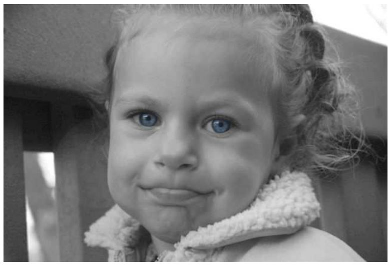
Sensorineural hearing loss, mild to moderate

Hyperacusis

Phonophobia

Abnormal brain auditory evoked responses (BAER)

Decreased or absent ipsilateral acoustic reflex response to maximum stimulation



Eyes

Stellate pattern of iris

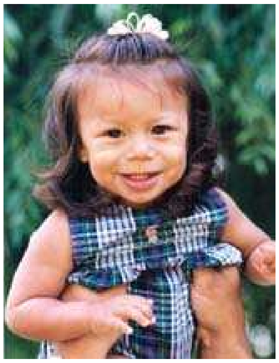
Nose

Depressed nasal bridge

Anteverted nares

Mouth

Thick lips



Teeth

Hypodontia

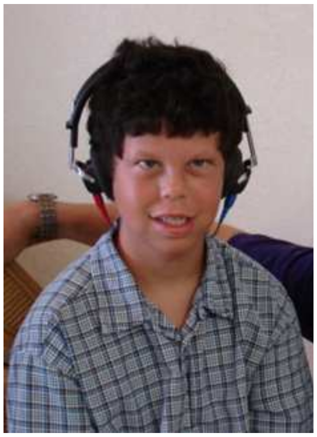
Microdontia

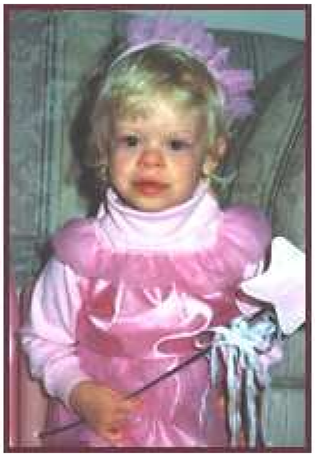
CARDIOVASCULAR :

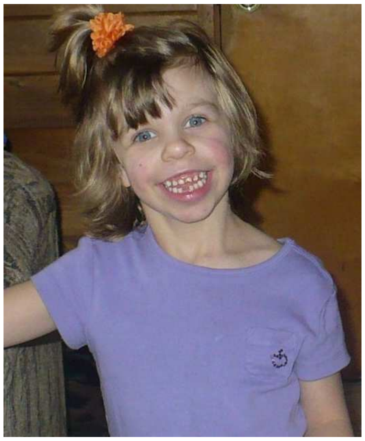
Heart

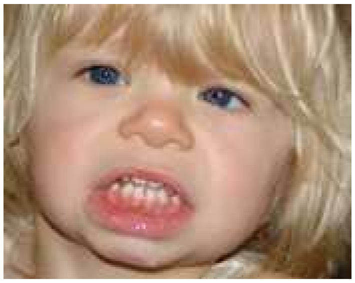
Supravalvular aortic stenosis

Valvular aortic stenosis









Bicuspid aortic valve
Mitral valve prolapse
Mitral regurgitation
Coronary artery stenosis
Pulmonary valve stenosis
Atrial septal defect
Ventricular septal defect

Vascular

Peripheral pulmonary artery stenosis
Systemic hypertension

RESPIRATORY :

Larynx

Vocal cord paralysis

CHEST :

Ribs, sternum, clavicles, and scapulae

Pectus excavatum

ABDOMEN :

External features

Inguinal hernia

Gastrointestinal

Chronic constipation
Diverticulosis

GENITOURINARY :

Kidneys

Small kidneys
Solitary kidney
Pelvic kidney
Nephrocalcinosis
Renal insufficiency
Renal artery stenosis

Ureters

Vesicoureteral reflux

Bladder

Bladder diverticula
Urethral stenosis
Recurrent urinary tract infections

SKELETAL :

Spine

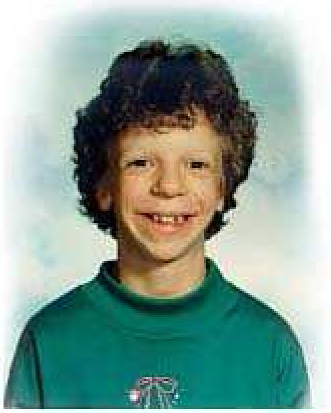
Kyphoscoliosis

Limbs

Joint limitation

Feet

Hallux valgus



NEUROLOGIC :

Central nervous system

Mental retardation (average IQ 56)

Relative sparing of language

Poor visual-motor integration (Range 41-80)

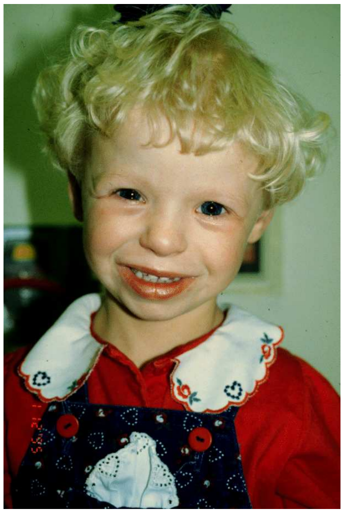
Hypersensitivity to sound

Behavioral/psychiatric manifestations

Attention deficit disorder

Cocktail party personality

Strong attraction to music



SKIN, NAILS, HAIR :

Nails

Hypoplastic nails

VOICE :

Harsh, brassy, or hoarse voice

ENDOCRINE FEATURES :

Hypercalcemia

LABORATORY ABNORMALITIES :

Hemizygous deletion at 7q11.23

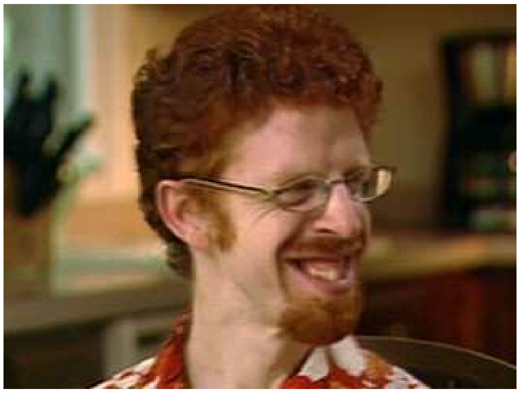
MISCELLANEOUS :

Incidence 1 in 8,000 live births

Main aspects of phenotype attributed to defects in GTF2IRD1 (604318) and GTF2I (601679)

MOLECULAR

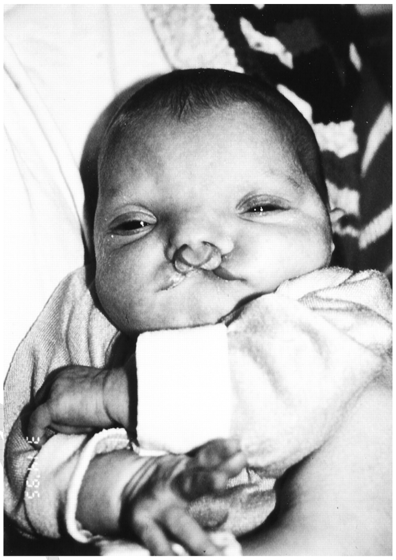
Contiguous gene syndrome involving mutation of genes on 7q11.2



WOLF-HIRSCHHORN SYNDROME; WHS / OMIM 2010

INHERITANCE:

Isolated cases



GROWTH:

Weight

Low birth weight

Other

Marked growth retardation

Failure to thrive

HEAD AND NECK:

Head

Microcephaly

Cranial asymmetry

Posterior midline scalp defects

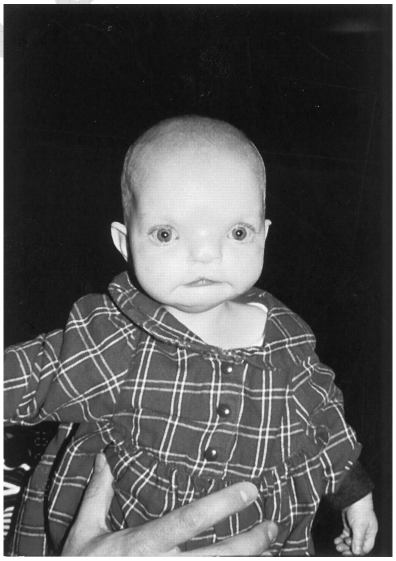
Face

Prominent glabella

Short philtrum

Micrognathia

High forehead



Ears

Preauricular tags

Preauricular pits

Hearing loss

Narrow external auditory canals

Eyes

Strabismus

Hypertelorism

Epicanthal folds

Exophthalmus

Ptosis

Rieger anomaly

Nystagmus

Iris coloboma

Corectopia

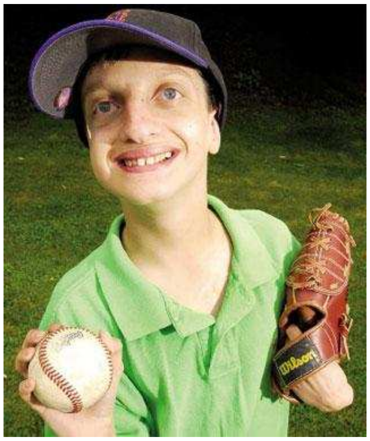
Nose

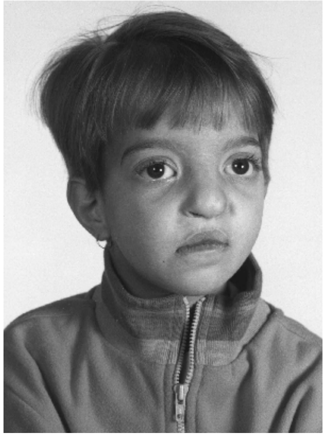
Wide nasal bridge

Beaked nose

Mouth

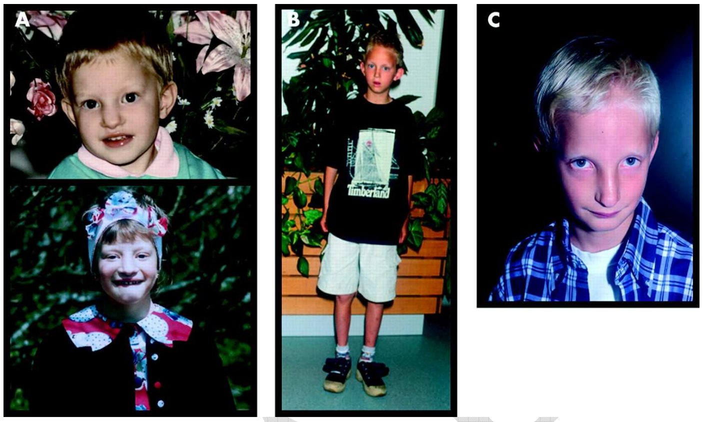
Cleft lip





ORIGINAL

Cleft palate
Downturned corners of mouth
Short upper lip
Teeth
Hypodontia
Neck
Webbed neck



CARDIOVASCULAR:

Atrial septal defect
Ventricular septal defect

CHEST:

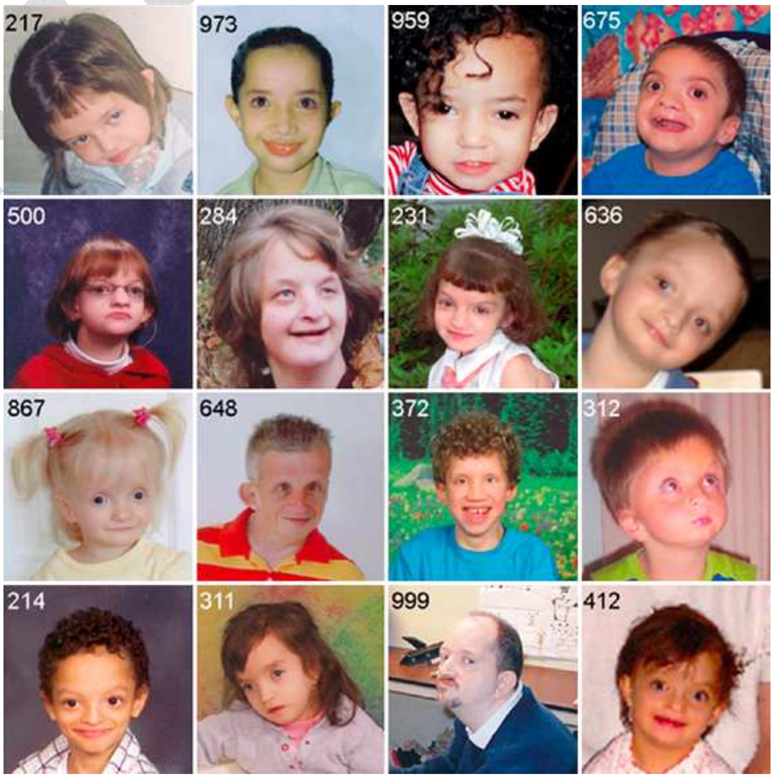
Ribs, sternum, clavicles, and scapulae
Sternal ossification center abnormalities
Fused ribs

ABDOMEN:

Absence of gallbladder
Accessory spleen
Malrotation of small bowel
Gastroesophageal reflux

GENITOURINARY:

External genitalia, male
Hypospadias
Internal genitalia, male
Cryptorchidism
Internal genitalia, female
Absent uterus

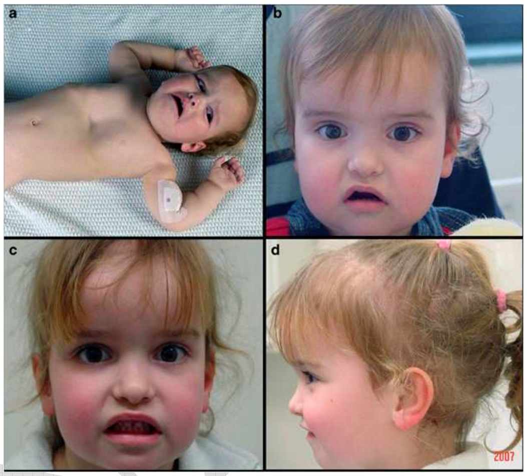


SKELETAL:

Delayed bone age
Spine
Sacral dimple
Sacral sinus
Scoliosis
Kyphosis
Fused vertebrae
Bifid vertebrae
Pelvis
Hip dislocation
Absence of pubic rami
Limbs

ORIGINAL

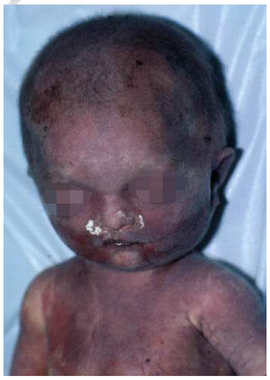
Thin limbs
Radioulnar synostosis
Hands
Transverse palmar creases
Accessory proximal metacarpal ossification centers



Feet
Talipes equinovarus
Metatarsus adductus
Polydactyly

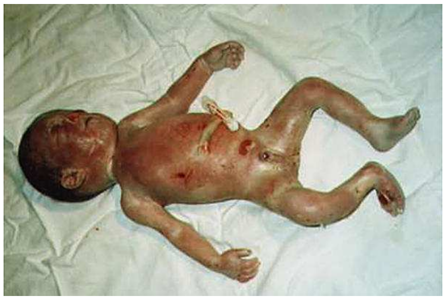
SKIN, NAILS, HAIR:

Posterior midline scalp defects
Sacral dimple
Transverse palmar creases
Hyperconvex fingernails
Low posterior hairline
High-arched eyebrows
Sparse medial eyebrows



NEUROLOGIC:

Severe mental retardation
Hypotonia
Seizures
Cavum septum pellucidum
Absent septum pellucidum
Interventricular cysts
Hydrocephalus



ENDOCRINE FEATURES:

Precocious puberty

PRENATAL MANIFESTATIONS:

Decreased fetal activity

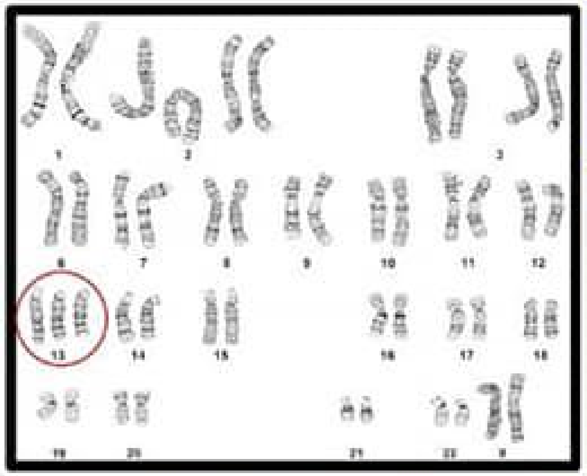
MISCELLANEOUS:

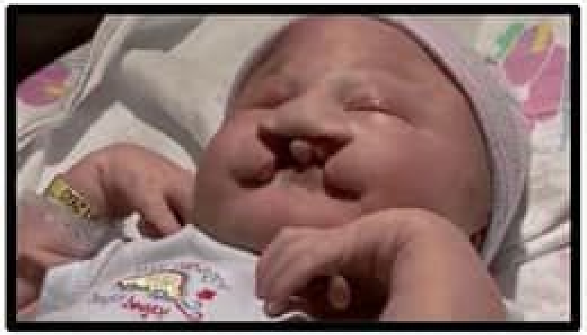
Sex ratio 2 females to 1 male
Partial deletion of short arm of chromosome 4.
De novo deletions in 8% of patients (preferentially paternally derived). 13% of cases secondary to familial translocation (often maternally derived) Size of deletion varies from cytogenetically visible deletions to undetectable cytogenetic deletions
FISH can be used to detect deletions of 4p16.3, the critical region for the phenotype. Approximately 35% of patients die during the first 2 years of life

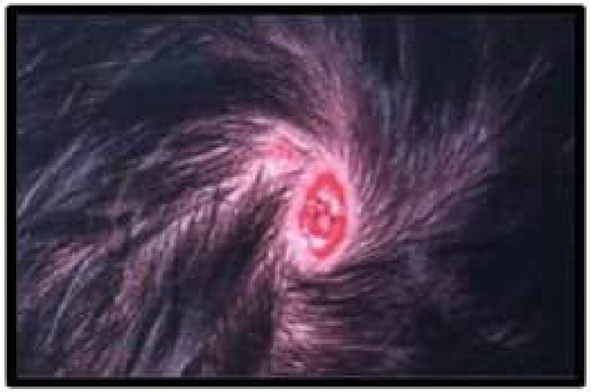
MOSTAFA ELBABA

ORIGIN

3) Trisomy 13 (Patau syndrome)







❖ Clinical features

- ✓ **Midline defect**
- ✓ **Aplasia cutis congenita**
- ✓ Microphthalmia
- ✓ Microcephaly
- ✓ Postaxial polydactyly
- ✓ Hypotonia
- ✓ Holoprosencephaly
- ✓ Hypoplastic / absent ribs
- ✓ Abdominal wall defect
- ✓ Deafness
- ✓ Colobomas
- ✓ Capillary hemangioma
- ✓ Genital anomalies
- ✓ Clenched fist

3rd most common autosomal trisomy

❖ Most common cardiac defect ?

1. **Ventricular septal defect (VSD)**
2. Atrial septal defect (ASD)
3. PDA

❖ Most common cause of death?

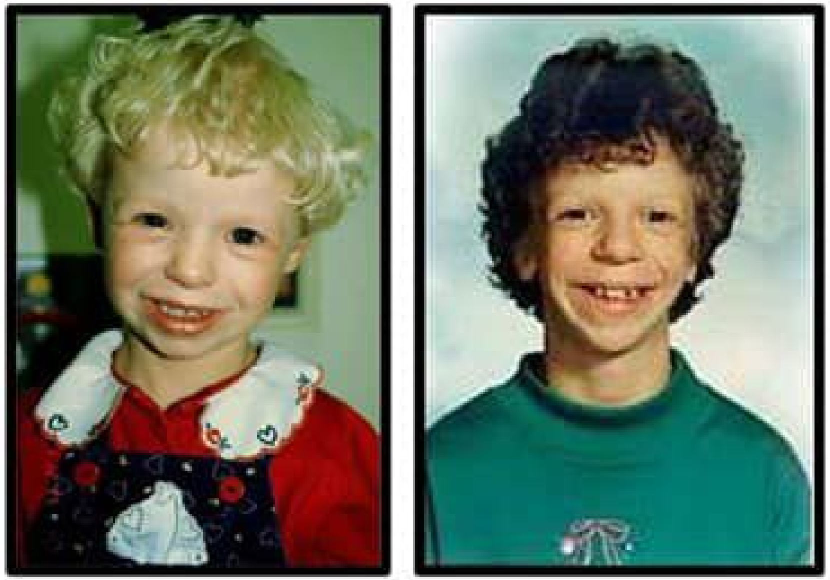
- ✓ Central apnea

Pediatric On Squares

❖ Prognosis

- ✓ 70% die in the 1st 3 months of life
- ✓ 95% die by 3 years of age
- ✓ Rarely reach up to 10 years

8) William Syndrome



❖ Clinical features

- ✓ Long philtrum (**Elfin face**)
- ✓ Broad mouth.
- ✓ Short nose with bulbous nasal tip.
- ✓ **Cocktail personality**
- ✓ Mental retardation
- ✓ Joint laxity

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❖ Mode of inheritance?

- ✓ Autosomal dominant
- ✓ Microdeletion 7q

❖ Laboratory finding ?

- ✓ Hypercalcemia

❖ Most common cardiac defect ?

- ✓ **Supravalvular aortic stenosis (80%)**
- ✓ Peripheral pulmonic stenosis
- ✓ Pulmonary valvular stenosis

❖ Eye problems ?

- ✓ Stellate irises
- ✓ Strabismus

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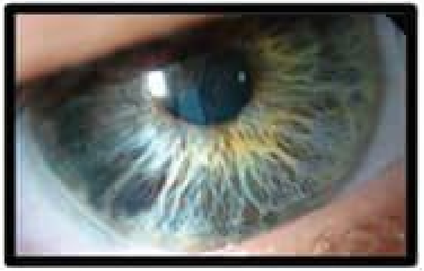
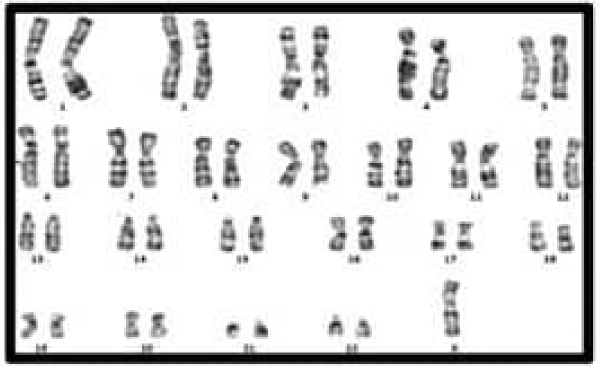
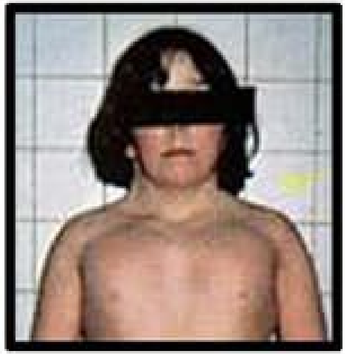
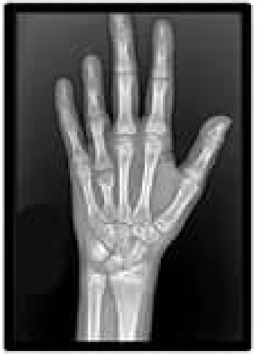
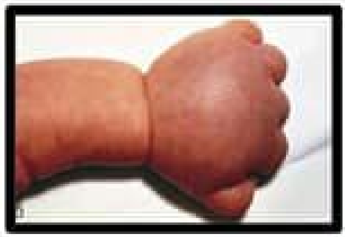


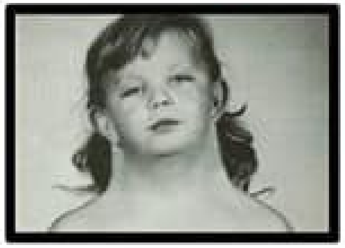
❖ **The AAP recommends annual cardiology evaluations for patients with Williams syndrome.**

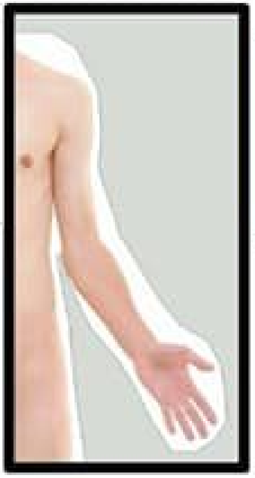












4) Turner Syndrome

❖ Clinical features

- ✓ Short stature
- ✓ Lymphedema of hands & feet
- ✓ Shield chest
- ✓ Cubitus valgus
- ✓ Low posterior hairline
- ✓ Posterior rotated ears
- ✓ Webbed neck
- ✓ Short 4th metacarpal bone
- ✓ Normal intelligence (except Math)

❖ What is the most consistent finding?

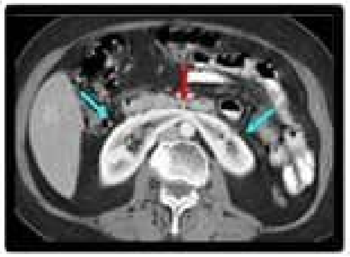
- ✓ Short stature (SHOX gene)
- ✓ Ovarian dysgenesis

❖ What is the most common cardiac defect?

1. Bicuspid aortic valve
2. Coarctation of aorta

❖ Labs finding ?

- ✓ High FSH
- ✓ High FSH/LH
- ✓ Low estradiol



❖ What is the most common renal anomaly ?

- ✓ Horseshoe kidney
- ✓ Double collecting system

❖ Increases risk of :

- ✓ Hypothyroidism
- ✓ Hashimoto disease
- ✓ Celiac disease
- ✓ Inflammatory bowel disease

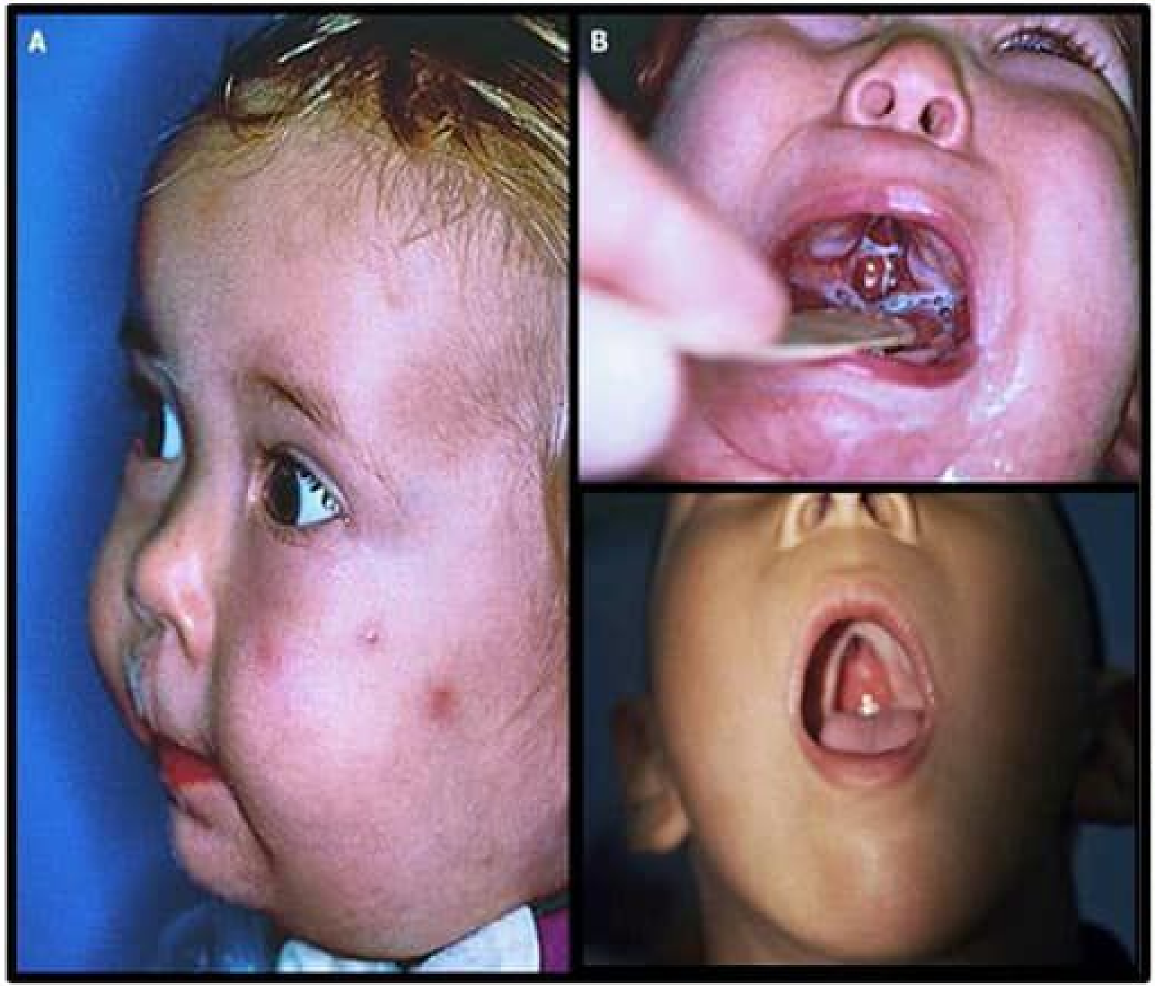
❖ Increases risk of which Malignancy ?

- ✓ Gonadoblastoma

❖ Treatment

- ✓ Growth hormone
- ✓ Estrogen therapy

29) Pierre Robin sequence (Pierre Robin syndrome)



Clinical features

- ✓ Mandibular hypoplasia
- ✓ Micrognathia
- ✓ Glossoptosis (backward displacement of the tongue)
- ✓ U shaped cleft palate
- ✓ Birdlike facial appearance.
- ✓ Upper airway obstruction

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❖ Mode of inheritance?

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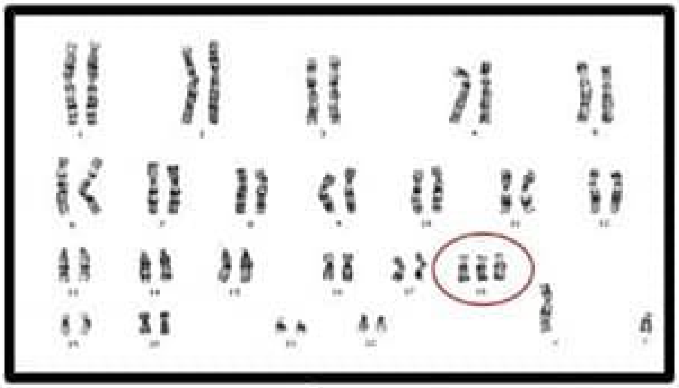
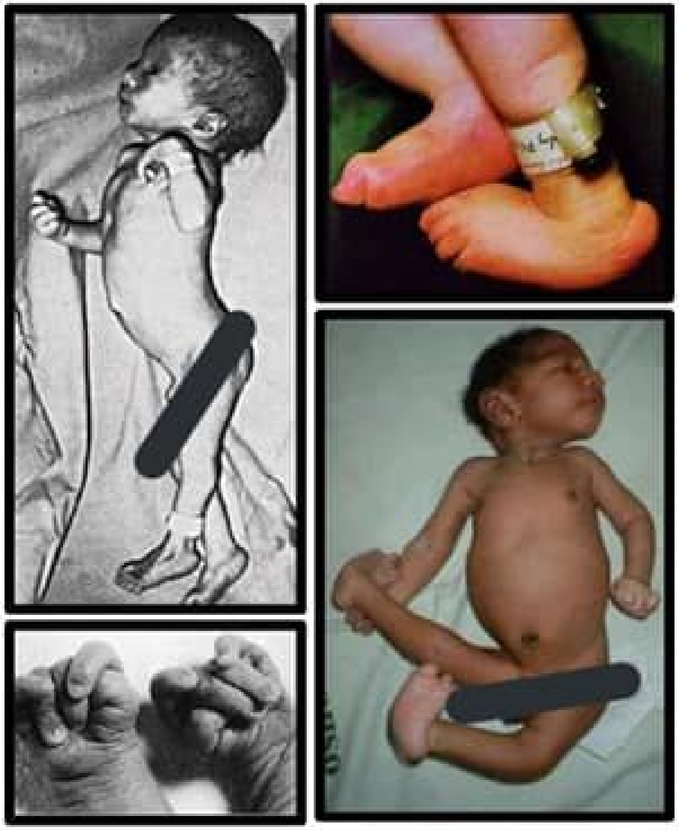
- ✓ De novo mutation
- ✓ SOX9 gene

❖ Most common cause of death?

- ✓ Upper airway obstruction

2) Trisomy 18 (Edwards syndrome)





- **Clinical features**
  - ✓ **Rocker bottom feet**
  - ✓ **Overlapping fingers**
  - ✓ **Clenched fist**
  - ✓ Short sternum
  - ✓ Hypoplastic nails
  - ✓ Hypoplastic nasal alae
  - ✓ IUGR
  - ✓ Intellectual disability
  - ✓ Microcephaly
  - ✓ Hypertonia
  - ✓ Prominent occiput
  - ✓ Micrognathia
  - ✓ Limited hip abduction
  - ✓ Cleft lip / palate

2nd most common autosomal trisomy

- **Most common cardiac defect ?**
  - ✓ **Ventricular septal defect (VSD)**
  - ✓ Atrial septal defect (ASD)
  - ✓ PDA

- **Most common cause of death?**
  - ✓ Central apnea

- **Prenatal screen lab finding?**
  - ✓ Low α feto protein
  - ✓ Low estriol
  - ✓ Low hCG

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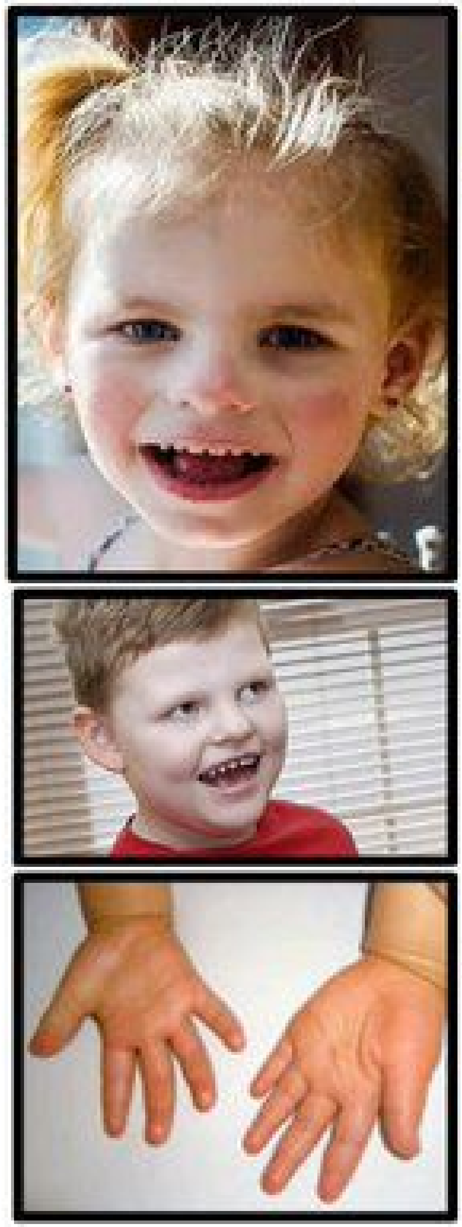
- **Prognosis**
  - ✓ 50% die in the 1st week of life
  - ✓ 90% die by 1 year of age

14) Angelman syndrome



- ❖ **Clinical features:**
  - ✓ Jerky ataxic movement “**Happy puppet**”
  - ✓ Inappropriate bouts of laughter
  - ✓ Excitable with hand flapping movement
  - ✓ Hypotonia
  - ✓ Fair hair
  - ✓ Seizure
  - ✓ Microcephaly
  - ✓ Severe Intellectual disabilities
  - ✓ Speech delay
  - ✓ Abnormal creases
  - ✓ Small and separated teeth

Pediatric On Squares
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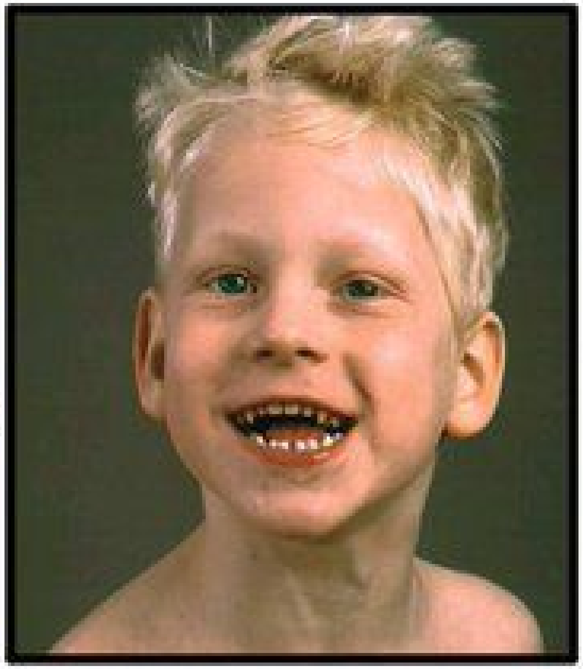
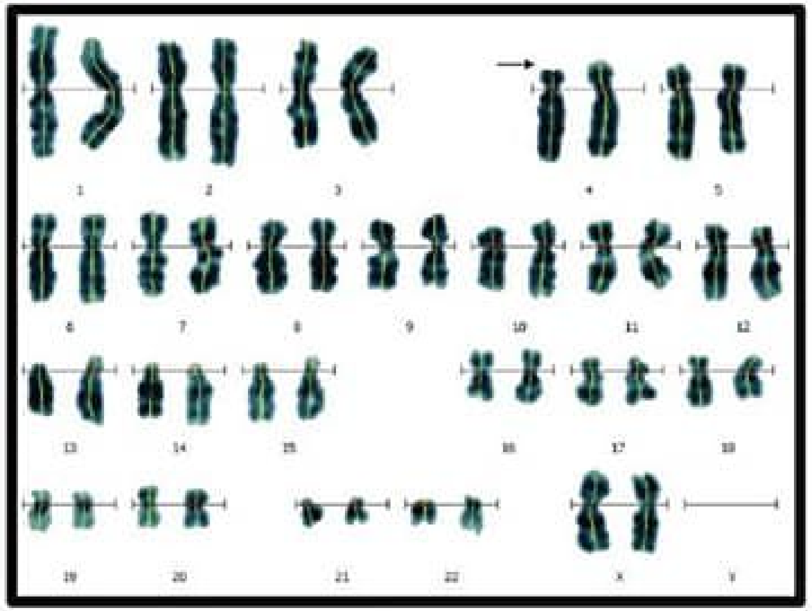
- ❖ **Mode of inheritance?**
  - ✓ Sporadic
  - ✓ Maternal derived deletion 15q11–13
  - ✓ Maternal UPD

- ❖ **Which medication should be avoided in seizure treatment?**
  - ✓ Carbamazepine
  - ✓ Vigabatrin



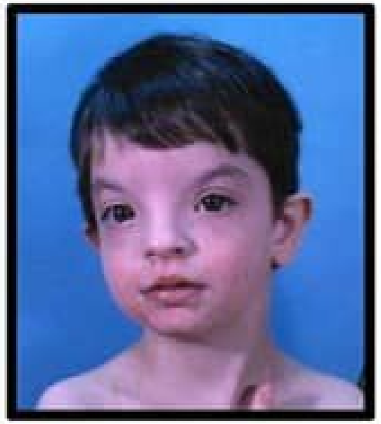
11) Wolf–Hirschhorn syndrome



❖ Clinical features:

- ✓ Microcephaly
- ✓ Hypertelorism
- ✓ Prominent glabella
- ✓ Frontal bossing
- ✓ **Greek helmet face**
- ✓ Beaked nose
- ✓ Hypotonia
- ✓ Seizures
- ✓ Cardiac defect

Pediatric On Squares



❖ Mode of inheritance?

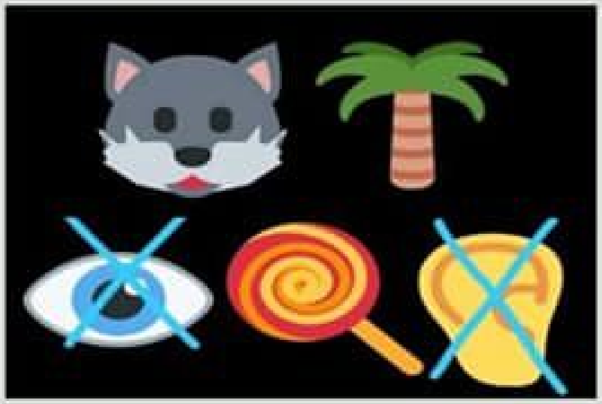
- ✓ De novo
- ✓ Deletion of the short arm of chromosome 4

❖ Laboratory finding ?

- ✓ IgA deficiency

≠

Wolf–Farm syndrome



❖ Clinical features:

- ✓ Diabetes insipidus
- ✓ Diabetes mellitus
- ✓ Blindness
- ✓ Deafness

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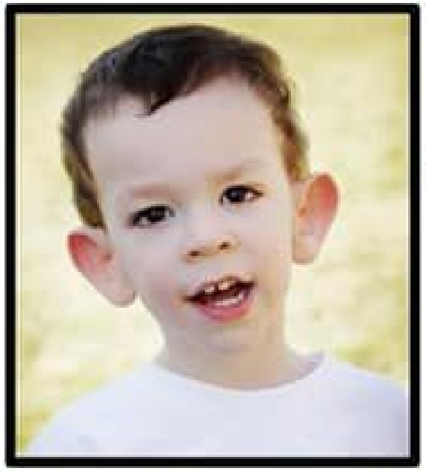
7) Fragile X Syndrome



❖ Clinical features

- ✓ Long narrow face
- ✓ Prominent jaw
- ✓ Big ears
- ✓ Large hand and feet
- ✓ **Macroorchidism**
- ✓ Hyperextensible joints
- ✓ Intellectual disability
- ✓ Behavioral problems (Autism, ADHD)
- ✓ Speech delay
- ✓ Pes planus (Flat foot)

Pediatric On Squares
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❖ Mode of inheritance?

- ✓ X-linked dominant inheritance
- ✓ > 200 **CGG** repeats in FMR1 gene

❖ What is the most common cardiac defect?

- ✓ **Mitral valve prolapse**

The most common form of **inherited** intellectual disability

But

The 2nd most common **genetic** intellectual disability (after trisomy 21)

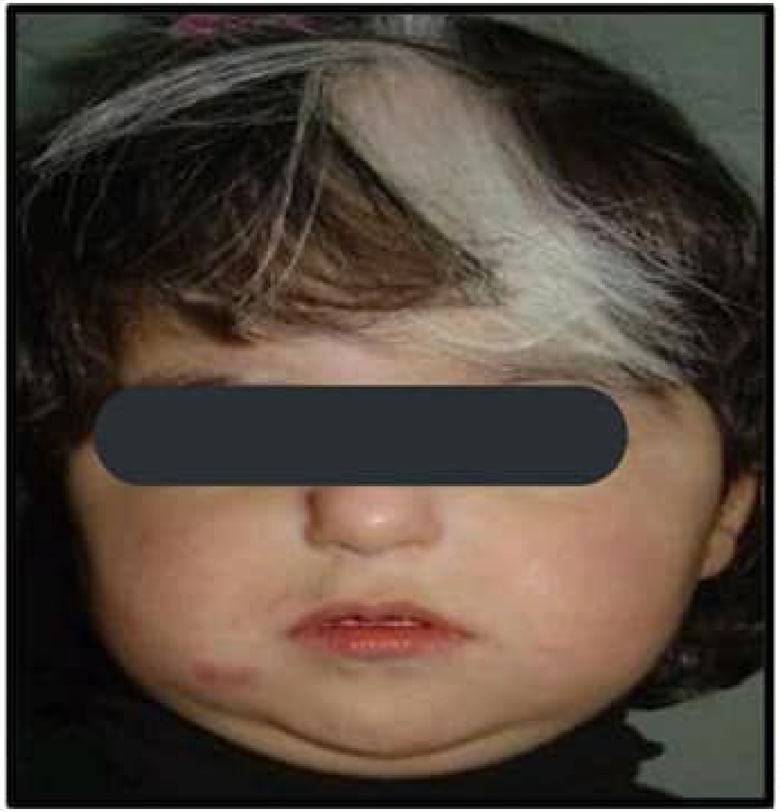
❖ How to confirm the diagnosis ?

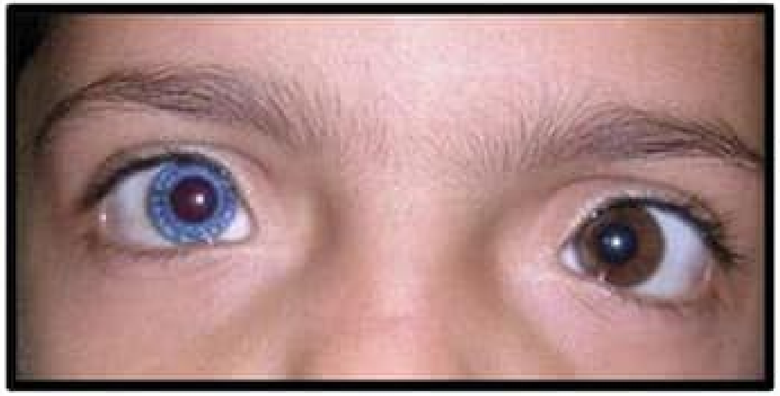
- ✓ Molecular genetic test for CGG allele repeat size

❖ Can a female have fragile X syndrome?

- ✓ Yes, but milder symptoms
- ✓ Premature ovarian failure

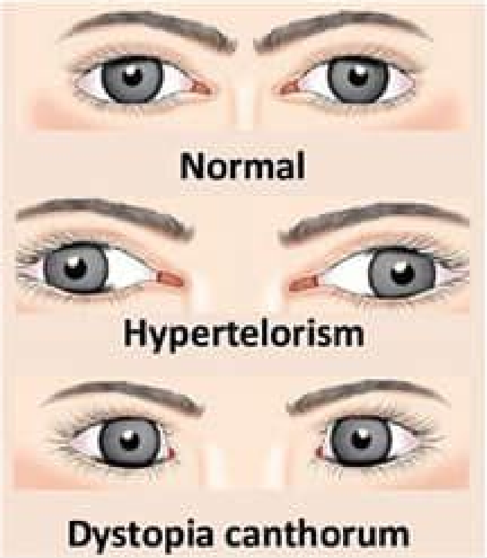
31) Waardenburg syndrome





Clinical features

- ✓ White forelock
- ✓ Square face
- ✓ Thin nose, wide nasal bridge
- ✓ Dystopia canthorum
- ✓ Heterochromia
- ✓ Sensorineural deafness
- ✓ Skin depigmentation


Normal
Hypertelorism
Dystopia canthorum

❖ **Mode of inheritance?**

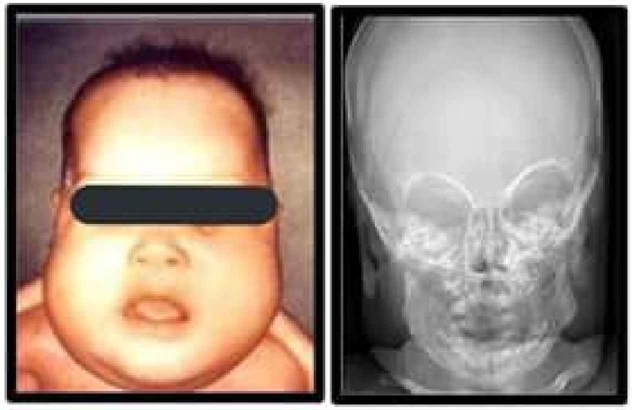
✓ Autosomal dominant

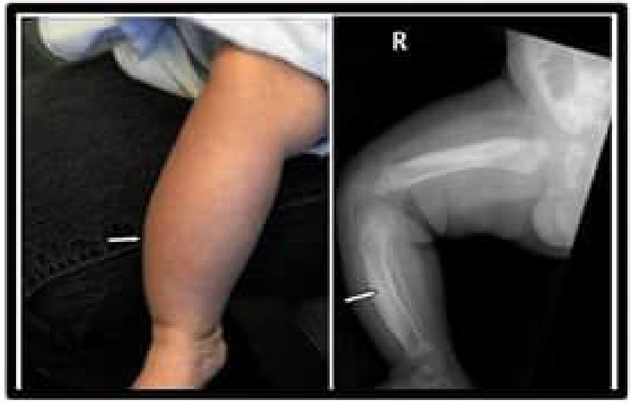
❖ **Most common gastrointestinal association?**

✓ Hirschsprung disease

Pediatric On Squares
@OnSquares

22) Infantile cortical hyperostosis (Caffey Disease)





The bone changes typically begin before six months of age and resolve by two years.

Clinical features

- Extreme irritability.
- Soft tissue swelling.
- Fever.
- Anorexia.
- Cortical thickening of bones.
- Pseudoparalysis

Differential diagnosis

- Osteomyelitis
- Hypervitaminosis A.
- Child abuse.
- Leukemia

Pediatric On Squares
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❖ Most common affected bone?

✓ **Mandible**

❖ Mode of inheritance?

✓ Autosomal dominant
✓ COL1A1 gene

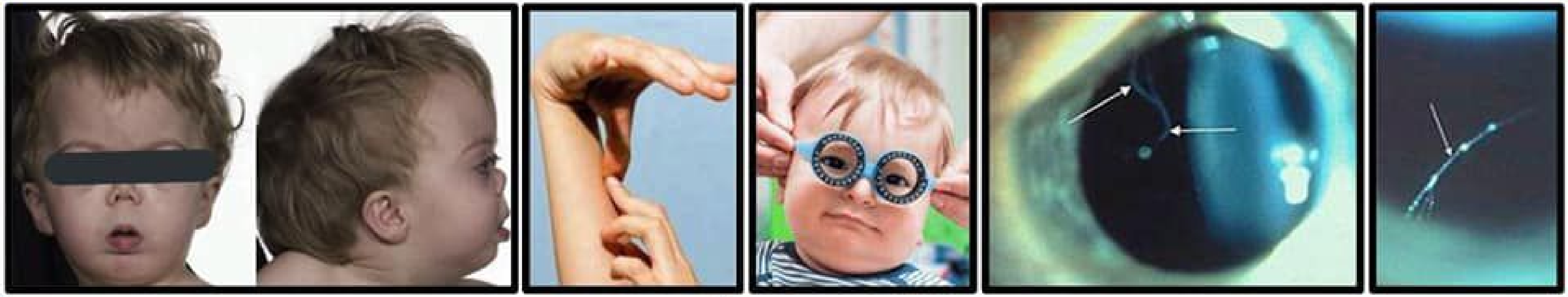
❖ Laboratory finding ?

✓ Leukocytosis
✓ Thrombocytosis
✓ High ESR
✓ High Alkaline phosphatase

❖ Prognosis

✓ Self-limited condition
✓ Deformities of the involved bones.

30) Stickler syndrome (hereditary arthroophthalmopathy)



Clinical features

- ✓ Pierre Robin sequence +
- ✓ Flat midface and nasal bridge
- ✓ Joint hypermobility
- ✓ Myopia
- ✓ Sensorineural deafness
- ✓ Cleft of the soft palate
- ✓ Arthritis

Pediatric On Squares
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❖ **Mode of inheritance?**

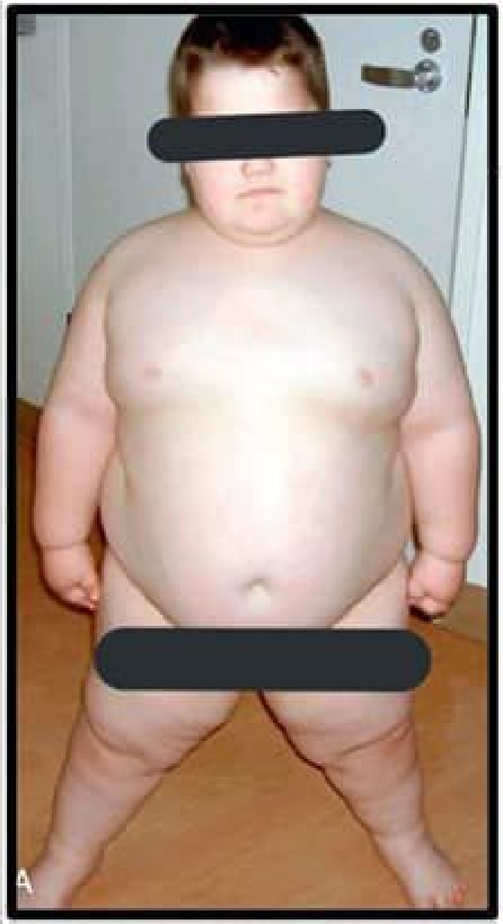
- ✓ Autosomal dominant

❖ **What is the pathognomonic eye finding?**

- ✓ Vitreous gel anomaly

❖ **What is ophthalmic emergency associated with stickler syndrome?**

- ✓ Retinal detachment



15) Prader Willi Syndrome (PWS)

- **Clinical features in infancy**
  - ✓ Hypotonia
  - ✓ feeding problems
- **Clinical features in childhood**
  - ✓ Hyperphagia
  - ✓ Central obesity
  - ✓ Hypogonadism
  - ✓ Short stature
  - ✓ Small hand and feet
  - ✓ Mild intellectual disability
  - ✓ Almond-shaped eyes
  - ✓ Behavioral disorder

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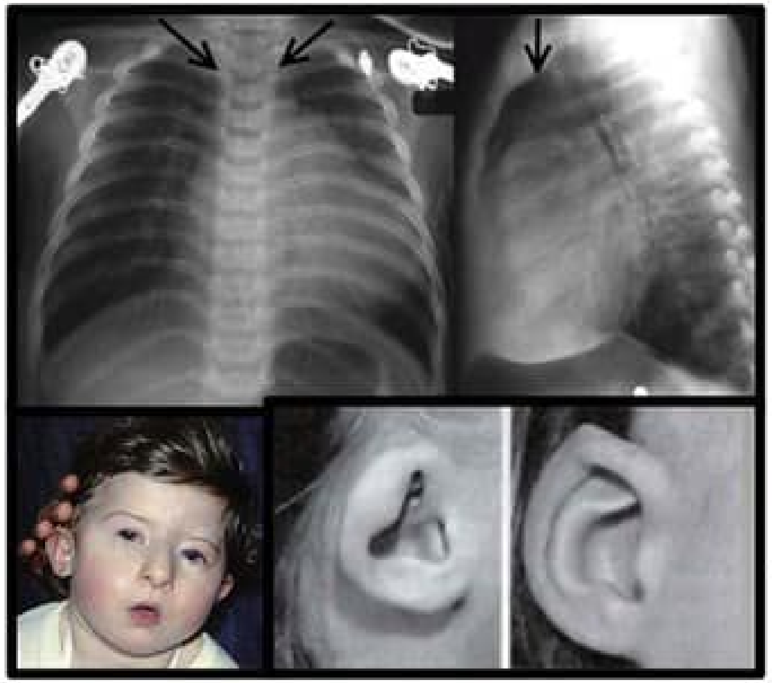
- **Mode of inheritance?**
  - ✓ Sporadic
  - ✓ Paternal derived deletion 15q11–13 (80%)
  - ✓ Maternal UPD (20%)

It is the most common syndromic form of obesity

- **Which medication had FDA approval to be used with PWS?**
  - ✓ Growth hormone therapy

- **Why they develop short stature, central obesity & hypogonadism ?**
  - ✓ Secondary to Hypothalamic and pituitary dysfunction

13) DiGeorge syndrome (Velocardiofacial syndrome)



❖ **Other names ?**
- ✓ 22q11.2 deletion syndrom
- ✓ Shprintzen syndrome

❖ **Mode of inheritance?**
- ✓ Autosomal dominant

Clinical features (CATCH 22)

- ✓ Cardiac defect
- ✓ Abnormal face (Hooded eyelids, ptosis, hypoplasia of auricles)
- ✓ Thymic hypoplasia (T cell abnormalities)
- ✓ Cleft palate
- ✓ Parathyroid aplasia / hypoplasia
- ✓ Hypernasal speech (Velopharyngeal incompetence)
- ✓ Hypotonia in infancy
- ✓ Learning disabilities & behavioral problems

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❖ **Common cardiac defect?**
- ✓ Interrupted aortic arch
- ✓ Truncus arteriosus
- ✓ Tetralogy of Fallot
- ✓ VSD

❖ **Laboratory finding ?**
- ✓ Hypocalcemia
- ✓ Low PTH
- ✓ Low IgG

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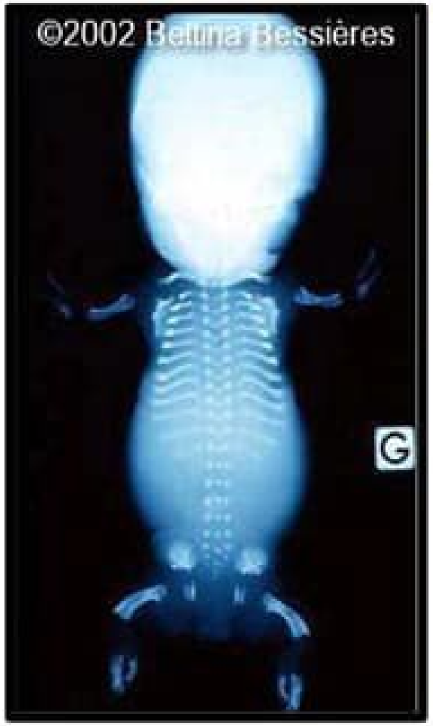
❖ **It is the MOST COMMON :**
- ✓ Microdeletion syndrome
- ✓ T-Cell disorder

❖ **Which vaccine should be avoided ?**
- ✓ live attenuated vaccine if immunodeficient

21) Thanatophoric Dysplasia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Clinical features

- Rhizomelic Shorting
- Small chest
- Absent sciatic notch.
- Platyspondyly (flattened vertebral bodies).
- French-telephone femurs.
- H-shaped vertebrae.
- Cloverleaf skull (severe craniosynostosis).

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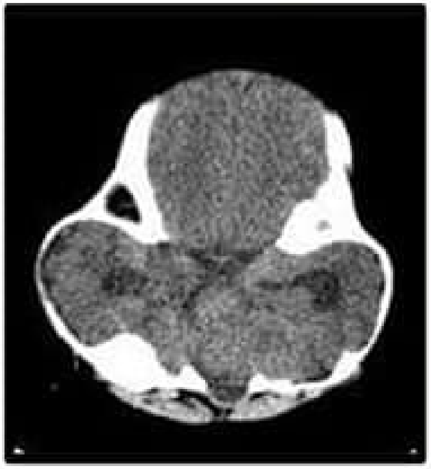
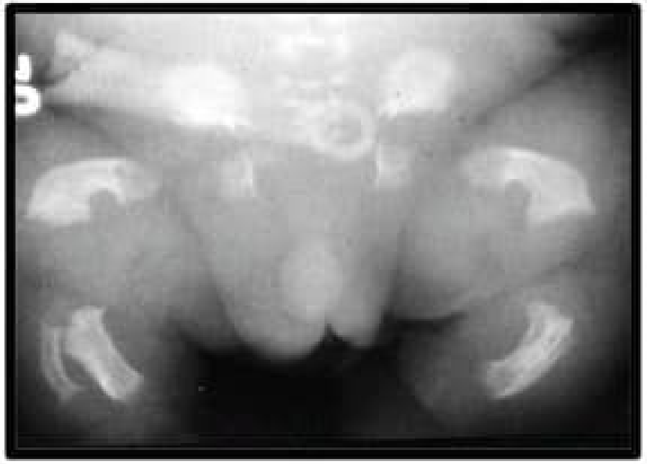
❖ **Mode of inheritance?**
- ✓ Autosomal Dominant
- ✓ Defect in FGFR-3

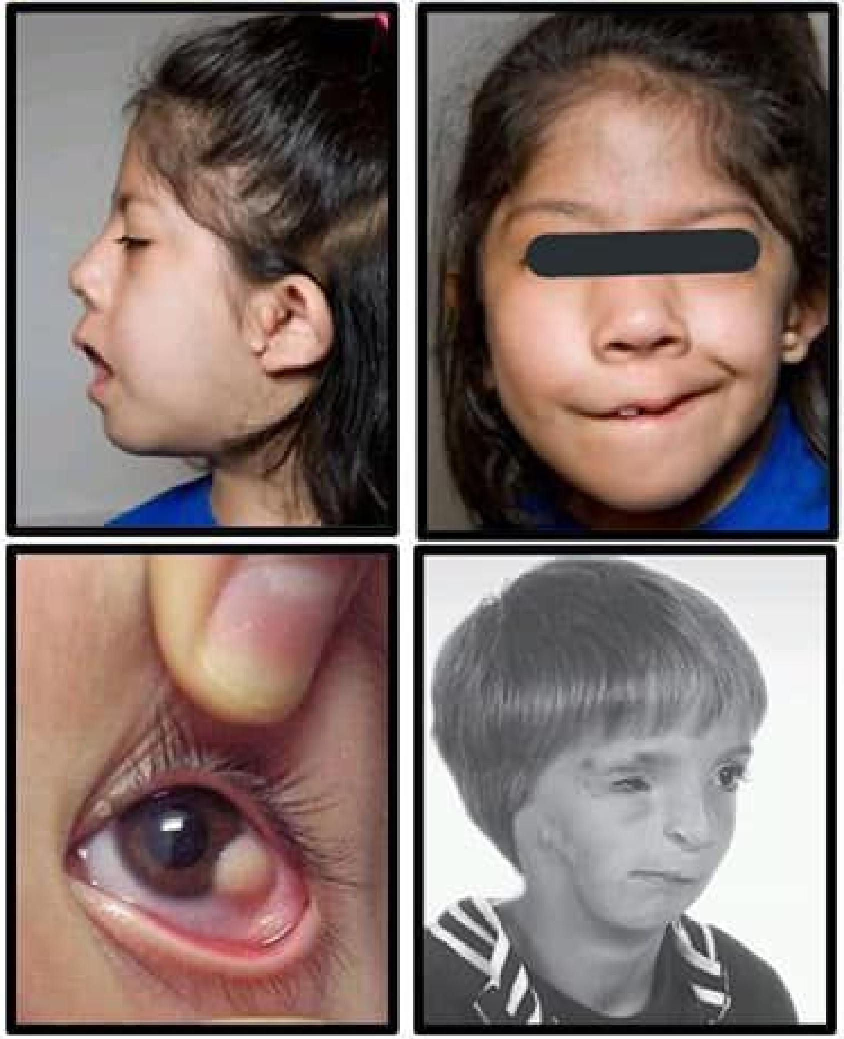
❖ **Most common cause of death?**
- ✓ Craniocervical junction compression
- ✓ Pulmonary hypoplasia



❖ **Types**
- Type I
  - Without cloverleaf skull
  - Telephone receiver femur
- Type II
  - With cloverleaf skull
  - Straight femur



27) Goldenhar syndrome (oculo-auriculo-vertebral spectrum)



Clinical features

- ✓ Facial asymmetry (hemifacial macrosomia)
- ✓ Microtia
- ✓ Preauricular tags
- ✓ Microphthalmia
- ✓ Limbal (Epibulbar) dermoid (Pathagnomic)
- ✓ Eyelid coloboma
- ✓ Facial nerve involvement leads to hypoplasia of the facial muscles.
- ✓ Hypoplasia or absence of the parotid gland.
- ✓ Vetebral anomalies (Hemivertebrae)
- ✓ Cardiac defect (VSD)

❖ **Mode of inheritance?**

- ✓ Sporadic
- ✓ Abnormal 1st and 2nd brachial arches

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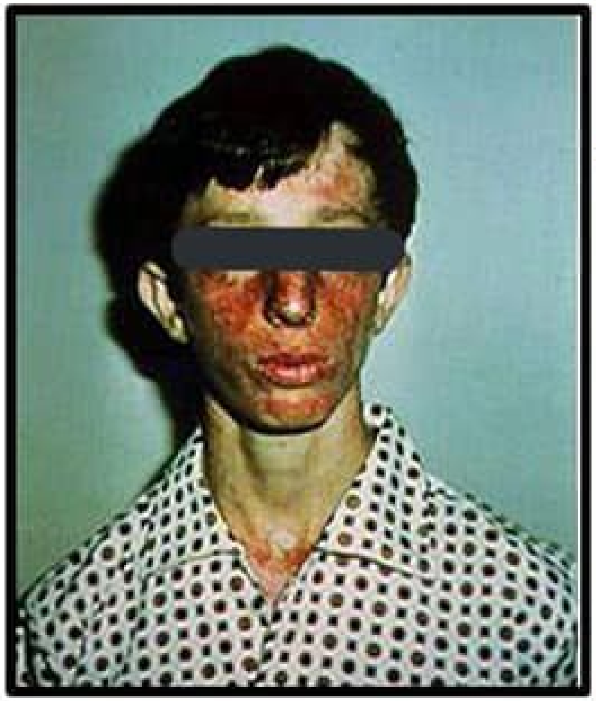

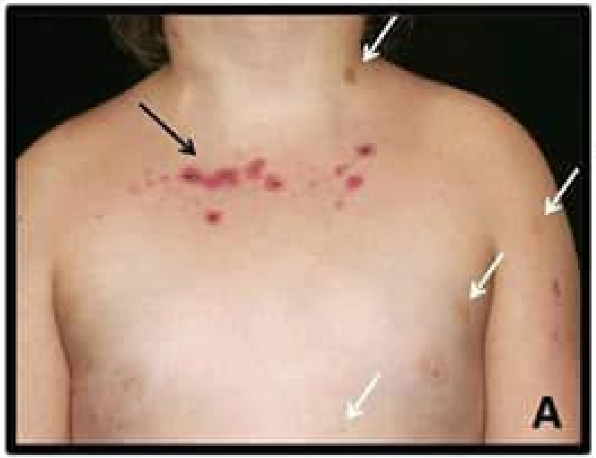

36) Bloom syndrome

❖ Clinical features

- ✓ Café-au-lait spots
- ✓ Photosensitive rash
- ✓ Long narrow face
- ✓ Prominent nose
- ✓ IUGR
- ✓ Microcephaly
- ✓ Short stature
- ✓ Infertility
- ✓ Immune deficiency

❖ Mode of inheritance?

- ✓ Autosomal recessive
- ✓ Due to chromosome instability

❖ Increase risk of:

- ✓ Malignancies
- ✓ Immunodeficiency

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❖ Laboratory finding ?

- ✓ Low immunoglobulin level
- ✓ Lymphopenia

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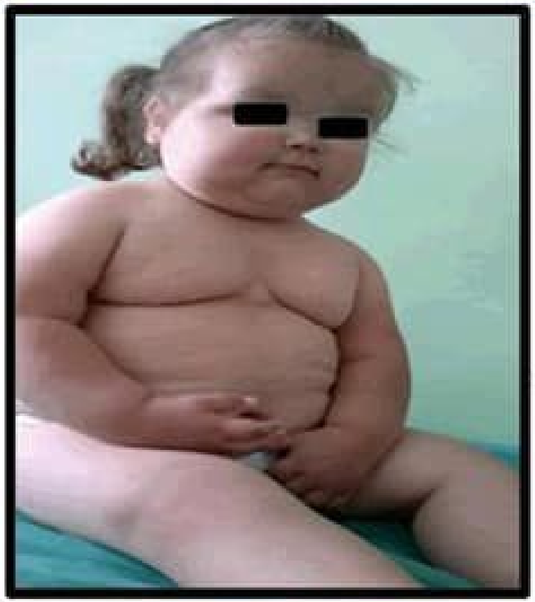
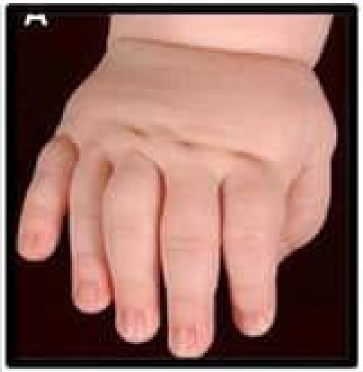
❖ Most common cause of death?

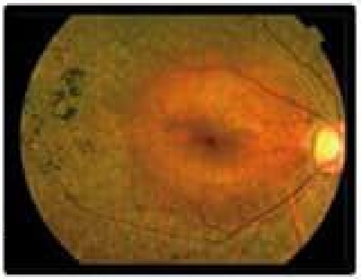
- ✓ Cancers
  - ▪ Mainly leukemia

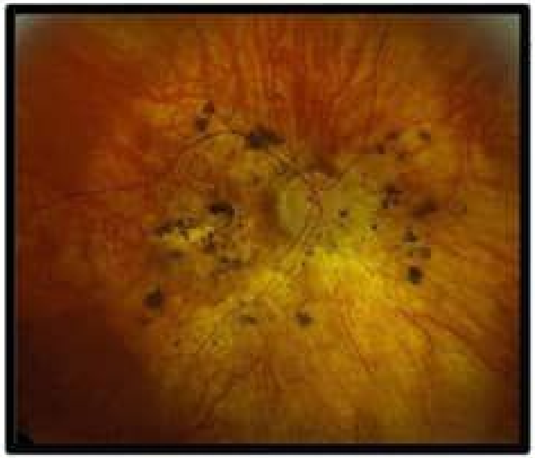
Avoid radiographs
Adequate sun protection

17) Bardet–Biedl syndrome (Laurence-Moon-Biedl syndrome)







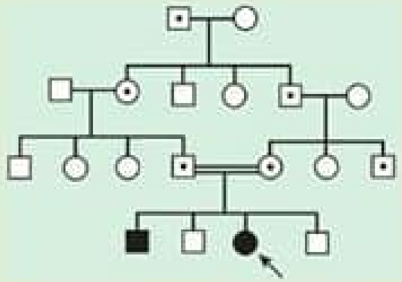


❖ Clinical features

- ✓ Obesity
- ✓ Postaxial polydactyly
- ✓ Hypogonadism
- ✓ Retinitis pigmentosa
- ✓ Rod-cone dystrophy
- ✓ Mental retardation
- ✓ Polyuria and polydipsia
- ✓ Renal anomalies

❖ Mode of inheritance?

- ✓ Autosomal recessive



❖ Most common gastrointestinal association?

- ✓ Hirschsprung disease

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❖ What is the cause of polyuria and polydipsia?

- ✓ Nephrogenic diabetes insipidus

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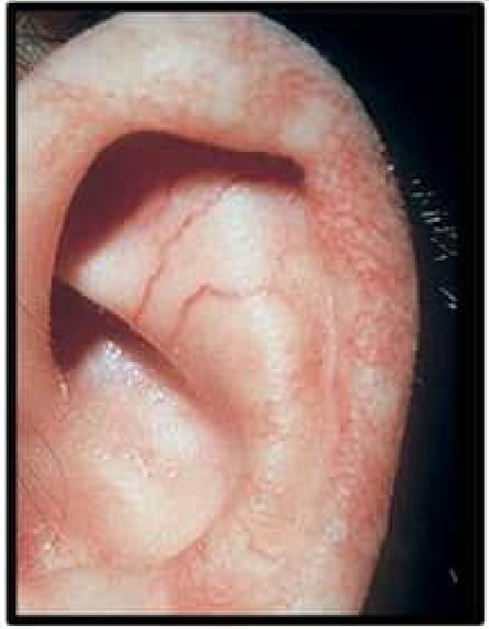
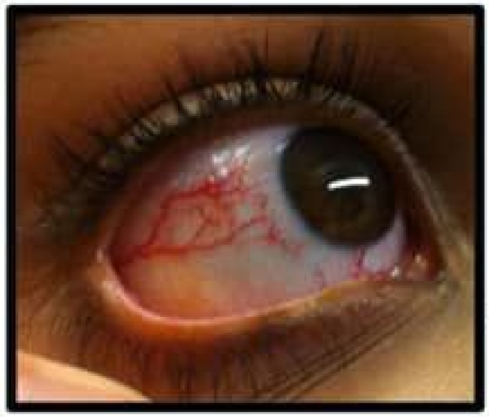
34) Ataxia Telangiectasia





❖ Clinical features

- ✓ Cerebellar ataxia
- ✓ Oculocutaneous telangiectasia
  - Bulbar conjunctivae.
  - Ears
  - Neck
  - Cubital fossae
- ✓ Recurrent infection
- ✓ Increase risk of malignancy

❖ Laboratory finding ?

- ✓ High serum alpha-fetoprotein (AFP)
- ✓ High carcinoembryonic antigen (CEA)
- ✓ Low IgA, IgG & IgE

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❖ What is the most consistent laboratory abnormality?

- ✓ High AFP

❖ Mode of inheritance?

- ✓ Autosomal recessive
- ✓ ATM gene
- ✓ Due to chromosome instability

❖ Which part of immune system is impaired?

- ✓ Both cellular and humoral immunity

- Associated with increase sensitivity to ionizing radiation

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14) Angelman syndrome

- **Clinical features:**
  - ✓ Jerky ataxic movement "**Happy puppet**"
  - ✓ Inappropriate bouts of laughter
  - ✓ Excitable with hand flapping movement
  - ✓ Hypotonia
  - ✓ Fair hair
  - ✓ Seizure
  - ✓ Microcephaly
  - ✓ Severe Intellectual disabilities
  - ✓ Speech delay
  - ✓ Abnormal creases
  - ✓ Small and separated teeth

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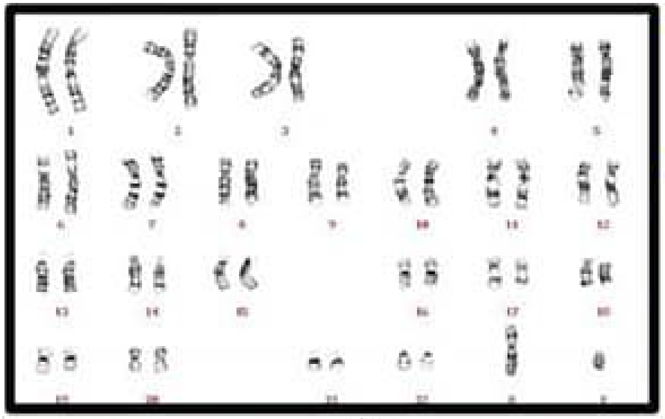
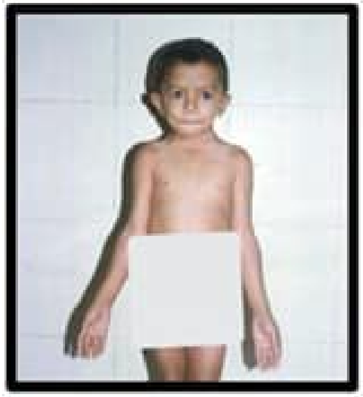
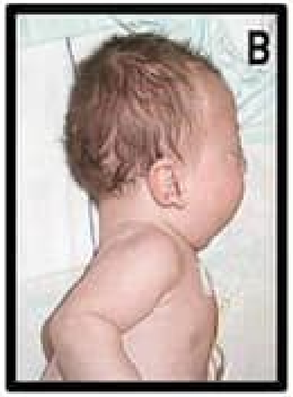
- **Mode of inheritance?**
  - ✓ Sporadic
  - ✓ Maternal derived deletion 15q11–13
  - ✓ Maternal UPD

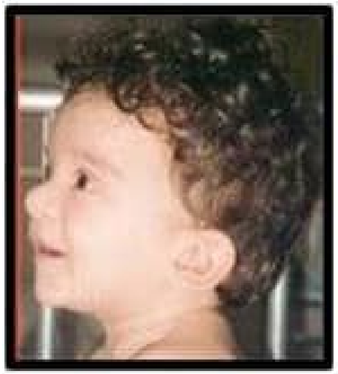
- **Which medication should be avoided in seizure treatment?**
  - ✓ Carbamazepine
  - ✓ Vigabatrin

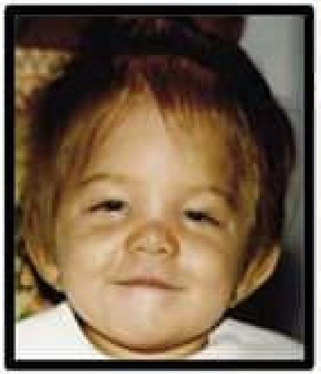
5) Noonan Syndrome











❖ Clinical features

- ✓ **Down slanting palpebral fissures**
- ✓ Short stature
- ✓ Shield chest
- ✓ Cubitus valgus
- ✓ Low posterior hairline
- ✓ Webbed neck
- ✓ Posterior rotated ears
- ✓ Cryptorchidism
- ✓ Intellectual disability
- ✓ Delayed puberty
- ✓ Ptosis

❖ Mode of inheritance?

- ✓ Autosomal dominant
- ✓ PTPN11 gene on 12q24
- ✓ Normal karyotype

❖ What is the most common cardiac defect?

1. Pulmonary stenosis
2. Hypertrophic cardiomyopathy

❖ Labs finding ?

- ✓ Clotting factor deficiencies
  - Mainly factor XI & XII
- ✓ Abnormal platelet count/function

❖ Increases risk of which Malignancy ?

- ✓ Acute lymphocytic leukemia (ALL)
- ✓ Chronic myeloid leukemia (CML)

❖ Treatment

- ✓ Growth hormone

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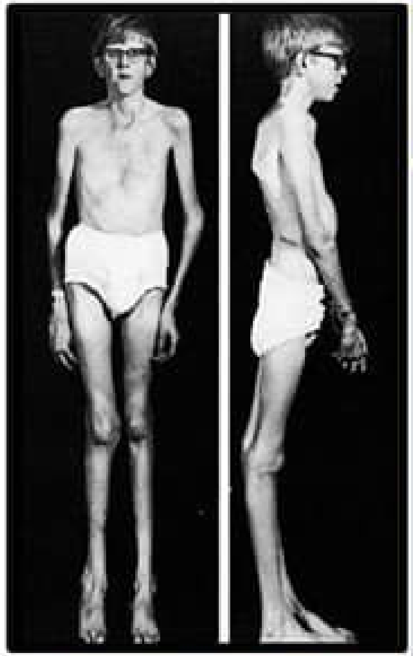
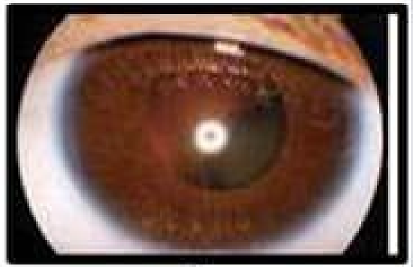
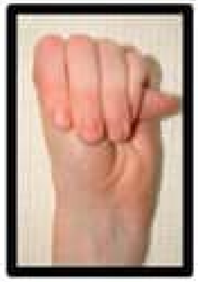
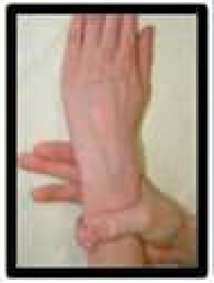
24) Marfan Syndrome









Clinical features

Major criteria:

- ✓ Ectopia lentis.
- ✓ Aortic dilatation or dissection.
- ✓ Family history

Systematic score features :

Wrist AND thumb sign	3
Wrist OR thumb sign	1
Pectus carinatum deformity	2
Pectus excavatum or chest asymmetry	1
Hindfoot deformity	2
Pes planus	1
Pneumothorax	2
Dural ectasia	2
Protrusio acetabuli	2
Reduced upper segment/lower segment ratio AND increased arm/height ratio AND no severe scoliosis	1
Scoliosis or thoracolumbar kyphosis	1
Reduced elbow extension	1
Facial features (3/5): dolichocephaly, enophthalmos, downslanting palpebral fissures, malar hypoplasia, retrognathia	1
Skin striae	1
Myopia >3 diopters	1
Mitral valve prolapse	1

❖ Mode of inheritance?

- ✓ Autosomal dominant
- ✓ FBN1 gene

❖ Monitoring?

- ✓ Annual echocardiogram.

How to confirm the diagnosis?

Ghent criteria

- 2 major criteria
- 1 major + FBN1 gene mutation
- 1 major + ≥7 more systematic score

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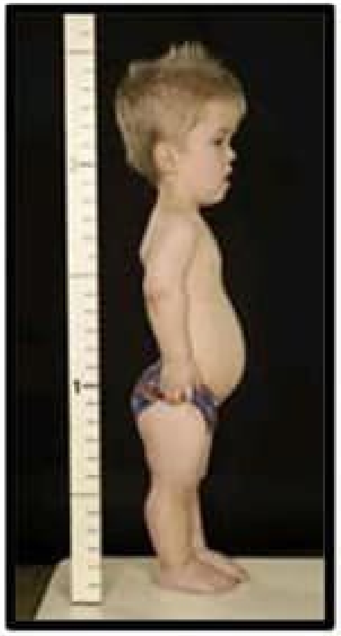
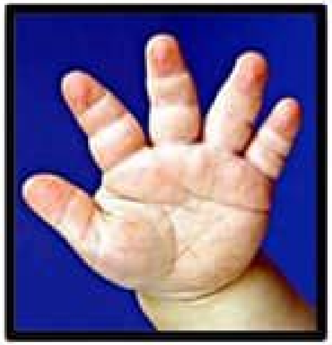
❖ Most common cardiac defect ?

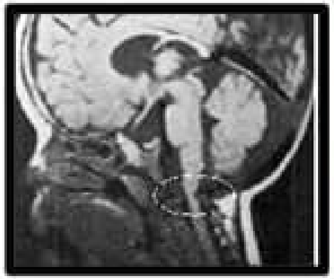
- ✓ **Mitral valve prolapse**
- ✓ Aortic root dilatation

❖ Most common cause of death?

- ✓ Cardiovascular complications
- ✓ Rupture aortic root dilatation







20) Achondroplasia

Clinical features

- Short stature below 3rd percentile.
- Rhizomelic Shorting (Short proximal long bones)
- Trident hands.
- Stenosis of foramen magnum.
- Macrocephaly.
- Midface hypoplasia
- Ice cream scoop shape femoral head.
- Squared-off iliac wings (Champagne glass sign).
- Increase risk of OSA & UAO.
- Delay in gross motor development.

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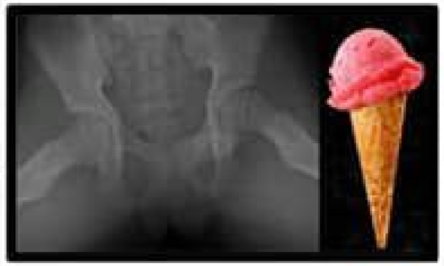
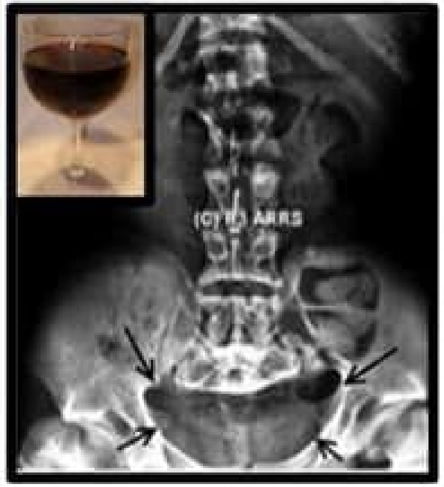


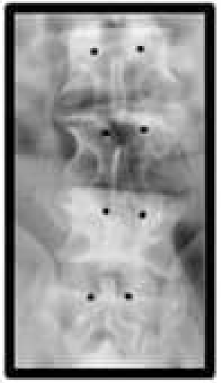


❖ **Mode of inheritance?**
- ✓ Autosomal Dominant
- ✓ Defect in FGFR-3

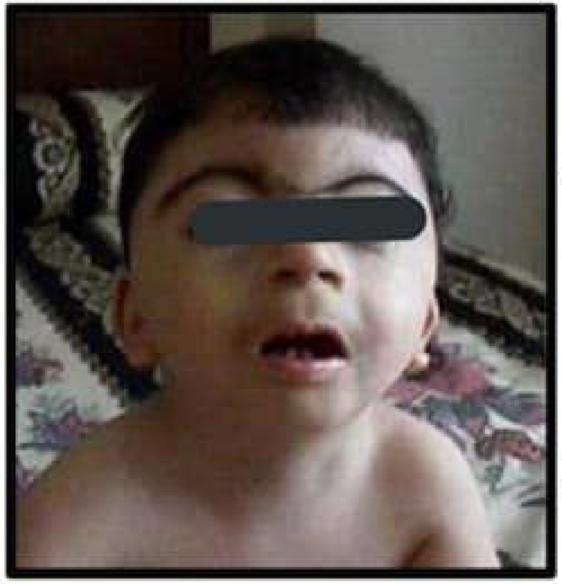
❖ **Clinic follow up ?**
- ✓ Head circumference.
- ✓ Hearing test annually.
- ✓ Polysomnography.

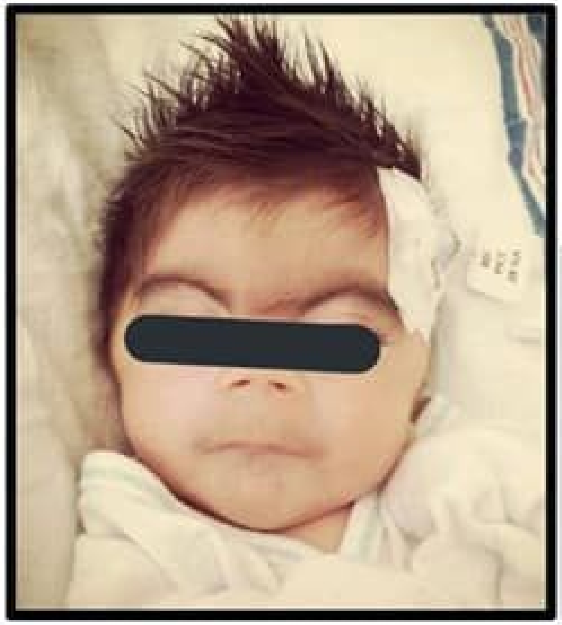
❖ **Most common cause of death?**
- ✓ Craniocervical junction compression

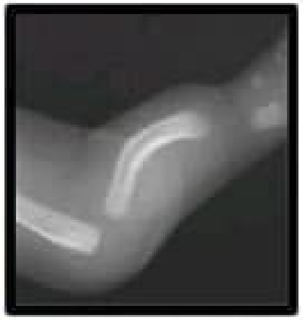
❖ **Spinal X-ray specific finding ?**
- ✓ Narrowed interpeduncular distances

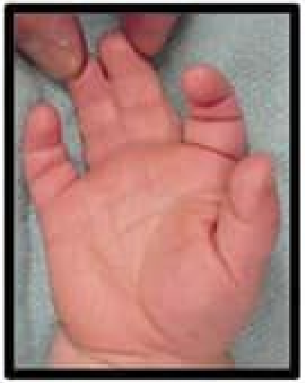


33) Cornelia de Lange Syndrome









❖ Clinical features

- ✓ Long eyelashes
- ✓ Bushy and arched eyebrows
- ✓ Hirsutism
- ✓ Low hairline
- ✓ Downward-turned mouth
- ✓ IUGR
- ✓ Short stature
- ✓ Thin upper lip
- ✓ Micromelia
- ✓ Lobster hand
- ✓ Syndactyly
- ✓ Ulnar dysplasia
- ✓ Mental retardation

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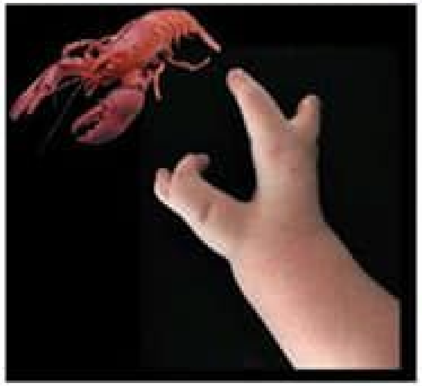
❖ Mode of inheritance?

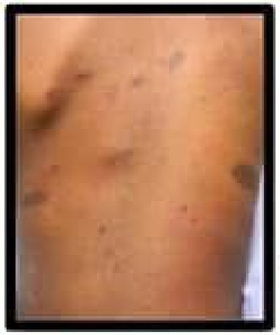
- ✓ Autosomal dominant

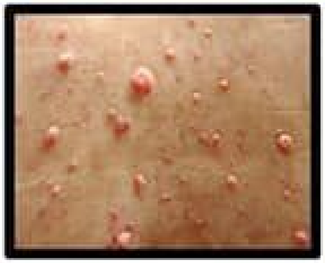
❖ Most common cardiac defect ?

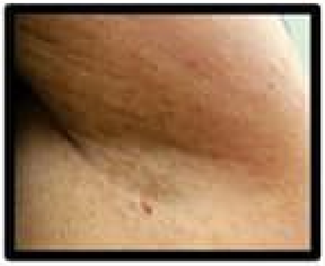
- ✓ Pulmonary stenosis
- ✓ VSD
- ✓ ASD
- ✓ CoA

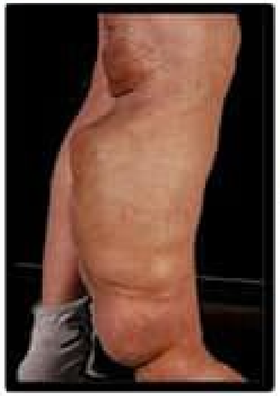


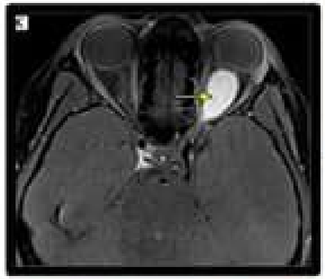
37) Neurofibromatosis type 1 (von Recklinghausen disease)

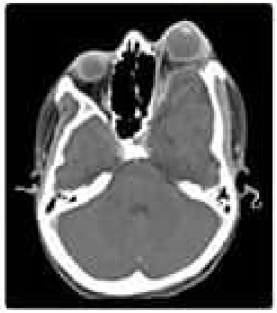


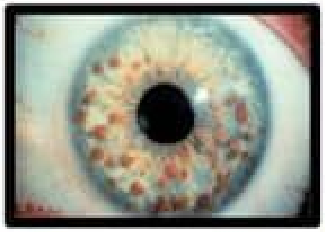












❖ **Diagnostic criteria** (≥ 2 of the following)

- ✓ ≥ 6 café-au-lait macules
  - > 5 mm in in prepubertal
  - > 15 mm in in postpubertal
- ✓ ≥ 2 neurofibromas or 1 plexiform neurofibroma
- ✓ Axillary or inguinal freckling (Crowe sign)
- ✓ Optic glioma
- ✓ ≥ 2 iris hamartoma (Lisch nodules)
- ✓ Distinctive bony lesion:
  - Sphenoid dysplasia, or
  - Tibial pseudoarthrosis, or
  - Cortical thickening of the long bone
- ✓ A first-degree relative with NF1

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❖ **What is 1st manifestation typically appears ?**

- ✓ Café-au-lait macules

❖ **What is most common type of benign tumor in NF1 ?**

- ✓ Neurofibromas

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❖ **Mode of inheritance?**

- ✓ AD (50%)
- ✓ De novo (50%)
- ✓ NF1 gene on chromosome 17

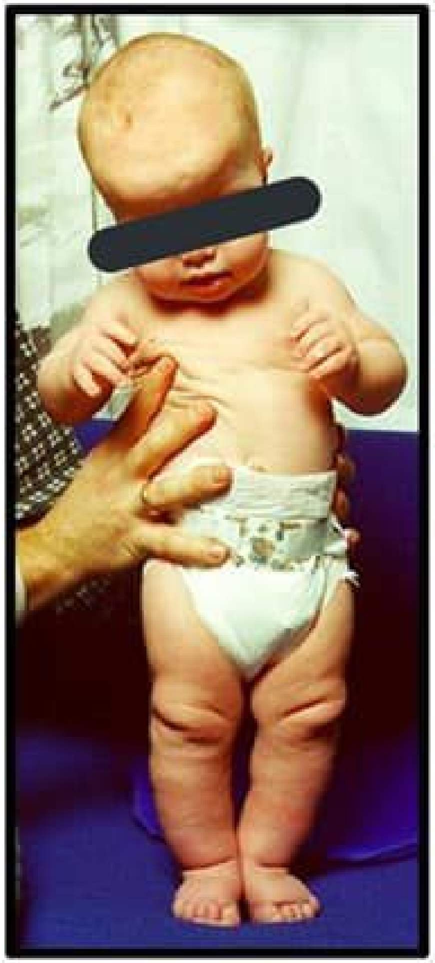
❖ **Increases risk of :**

- ✓ **Malignancies**
- ✓ Primary HTN
- ✓ Learning disabilities
- ✓ Seizures

❖ **Follow up :**

- ✓ Annual vision exam
- ✓ BP monitoring
- ✓ Annual full physical examination
- ✓ Tumor surveillance

18) Sotos syndrome (cerebral gigantism)



❖ Clinical features

- ✓ Large for gestational age
- ✓ Excessive growth in 1st year of life
- ✓ Large head , frontal prominence
- ✓ **Large hand and feet**
- ✓ **Premature tooth eruption**
- ✓ Intellectual disability
- ✓ Behavioral problems (Autism)
- ✓ Seizure
- ✓ Hypotonia
- ✓ Monotone voice

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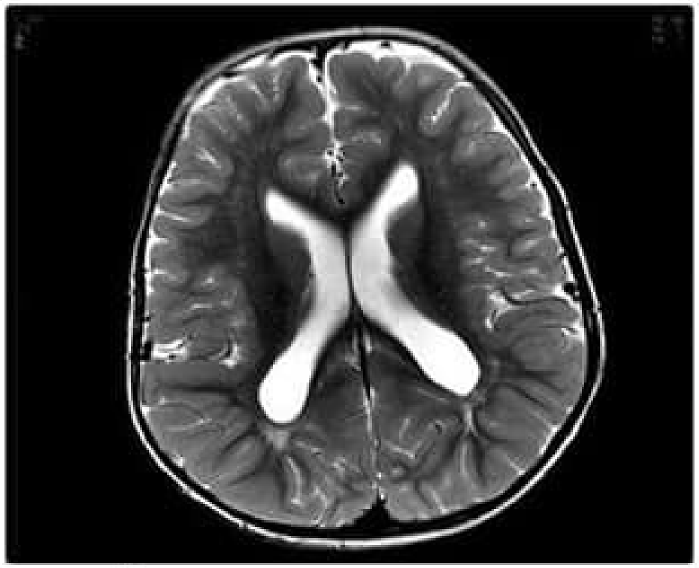
❖ Radiological finding ?

✓ Ventriculomegaly



❖ Mode of inheritance?

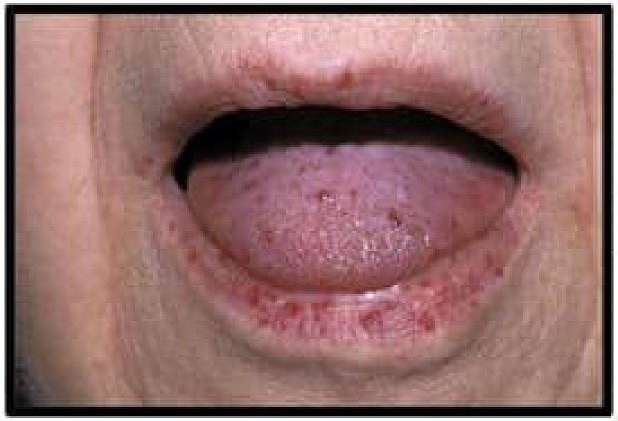
- ✓ Autosomal dominant

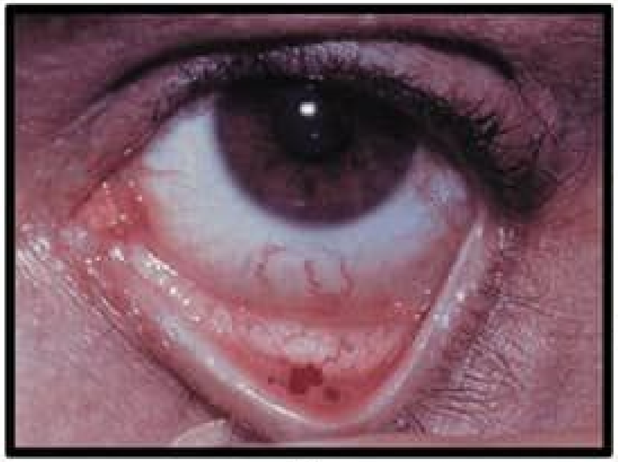
❖ Increases risk of which Malignancies ?

- ✓ Wilms tumor
- ✓ Hepatic carcinoma

❖ Prognosis

- ✓ Normal life expectancy
- ✓ Developmental delay





35) Osler Weber Rendu Syndrome (Hereditary hemorrhagic Telangiectasia)

❖ Clinical features

- ✓ Telangiectasia (lips, gingiva, tongue, palate and palpebral conjunctiva)
- ✓ Recurrent epistaxis (Night time)
- ✓ Vascular malformation (Lung, liver, GI & brain)

❖ Mode of inheritance?

- ✓ Autosomal dominant

❖ Complications ?

- ✓ Intracranial hemorrhage
- ✓ Pulmonary hemorrhage
- ✓ GI bleeding

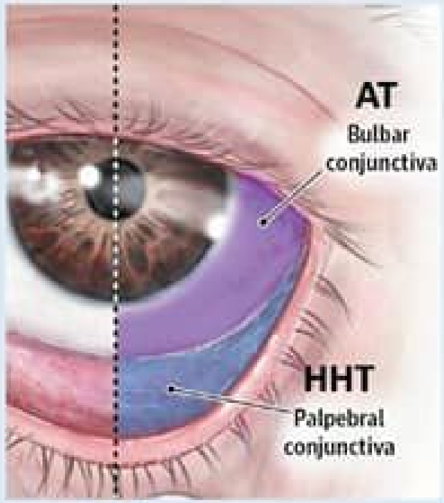
Pediatric On Squares

The most common cause of pulmonary arteriovenous malformation

Conjunctival finding in Hereditary hemorrhagic Telangiectasia (HHT)

VS

Ataxia Telangiectasia (AT)



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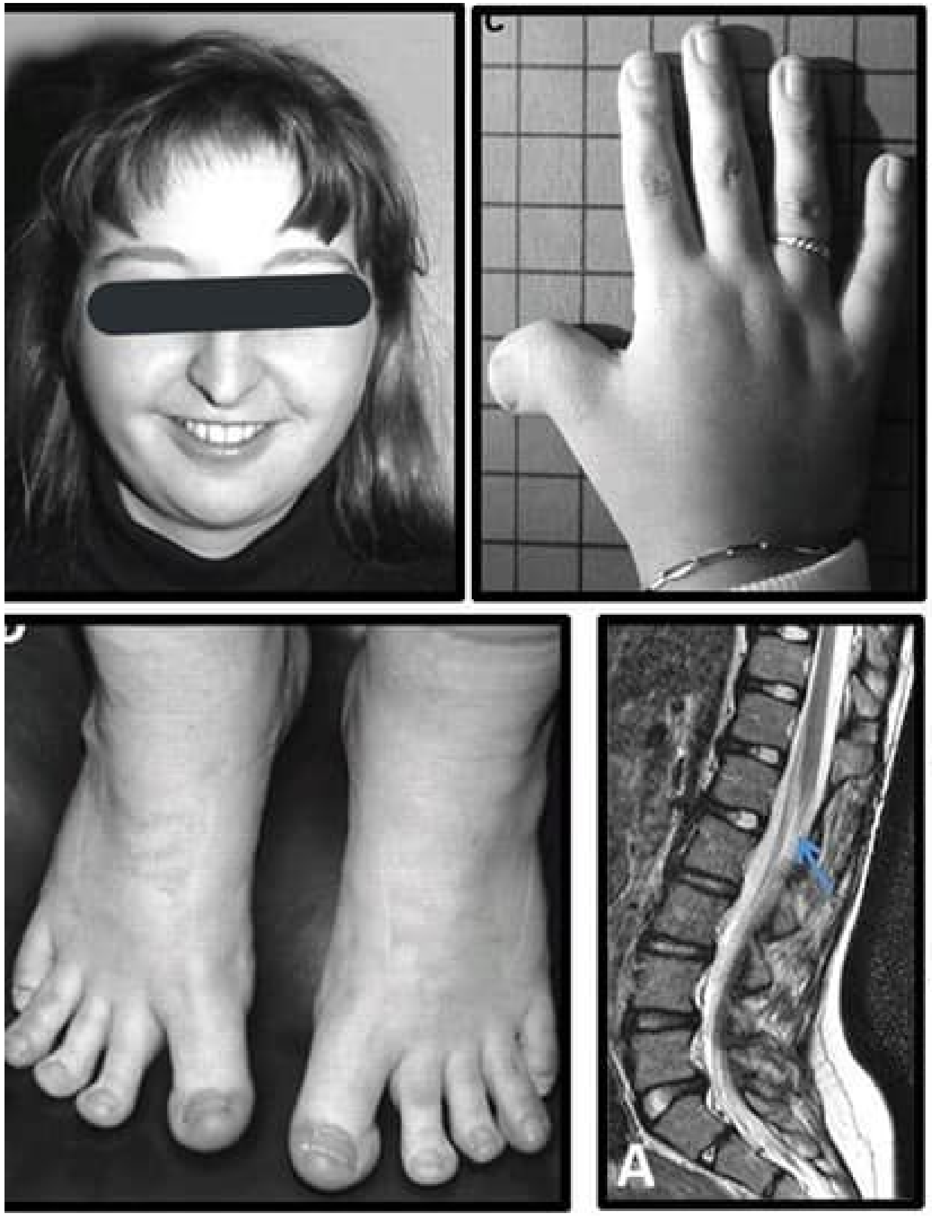

12) Rubinstein Taybi Syndrome

❖ **Clinical features**

- ✓ **Broad thumbs and great toes**
- ✓ **Prominent nasal septum , beaked nose**
- ✓ Microcephaly
- ✓ Large nails
- ✓ Long eyelashes
- ✓ Spinal cord tethering
- ✓ Cardiac defect
- ✓ Growth & mental retardation

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❖ **Mode of inheritance?**

- ✓ Autosomal dominant
- ✓ Microdeletion 16q

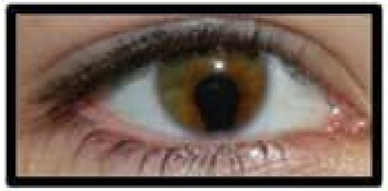
❖ **What is the most common cardiac defect?**

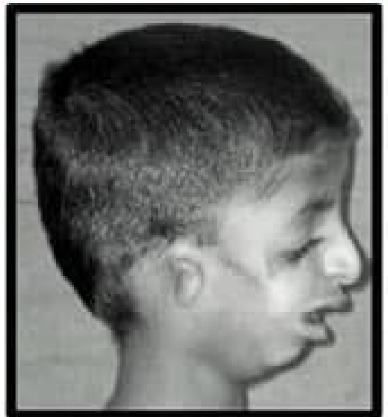
- ✓ Ventricular septal defect (VSD)

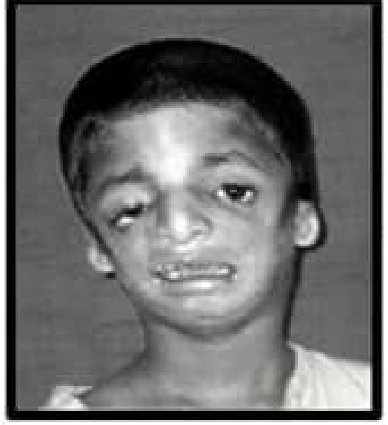
⚠ **CAUTION !!**

Rubinstein taybi syndrome have an increase risk of complications from anesthesia

26) Treacher Collins Syndrome (Mandibulofacial Dysostosis)







Clinical features

- ✓ Zygomatic and mandibular bone hypoplasia
- ✓ Eyelid colobomas
- ✓ Sparse eye lashes
- ✓ Microretrognathia
- ✓ Choanal atresia
- ✓ Microtia
- ✓ Conductive hearing loss
- ✓ Cleft lip / palate

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❖ Most common neonatal problem?

- ✓ Airway difficulties

❖ What is the level of intelligence ?

- ✓ Normal

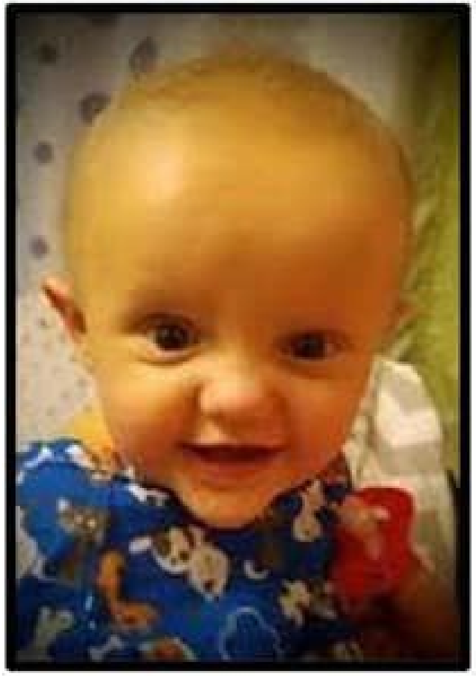
❖ Mode of inheritance?

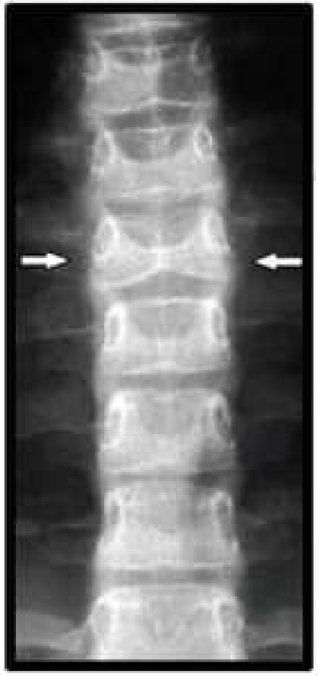
- ✓ Autosomal dominant
- ✓ TCOF1 gene

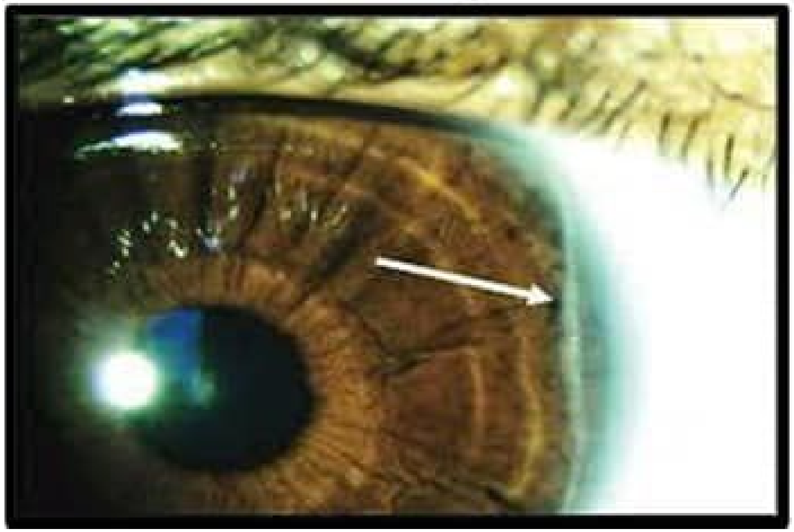
❖ Clinic follow up ?

- ✓ Vision assessment
- ✓ Hearing assessment
- ✓ Feeding difficulties
- ✓ Speech therapy
- ✓ Psychosocial therapy

9) Alagille syndrome







❖ Clinical features

- ✓ **Triangular face with pointed chin**
- ✓ Long nose
- ✓ Cholestatic jaundice
- ✓ **Posterior embryotoxon**
- ✓ **Butterfly vertebrae**

Liver biopsy show

↓

Paucity of bile duct

❖ Mode of inheritance?

- ✓ Autosomal dominant
- ✓ 20p12 deletion
- ✓ JAG1 gene

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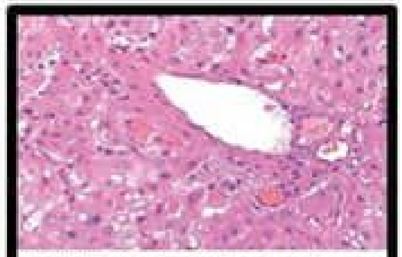


Paucity of intrahepatic bile duct. No bile duct is seen in Alagille syndrome.

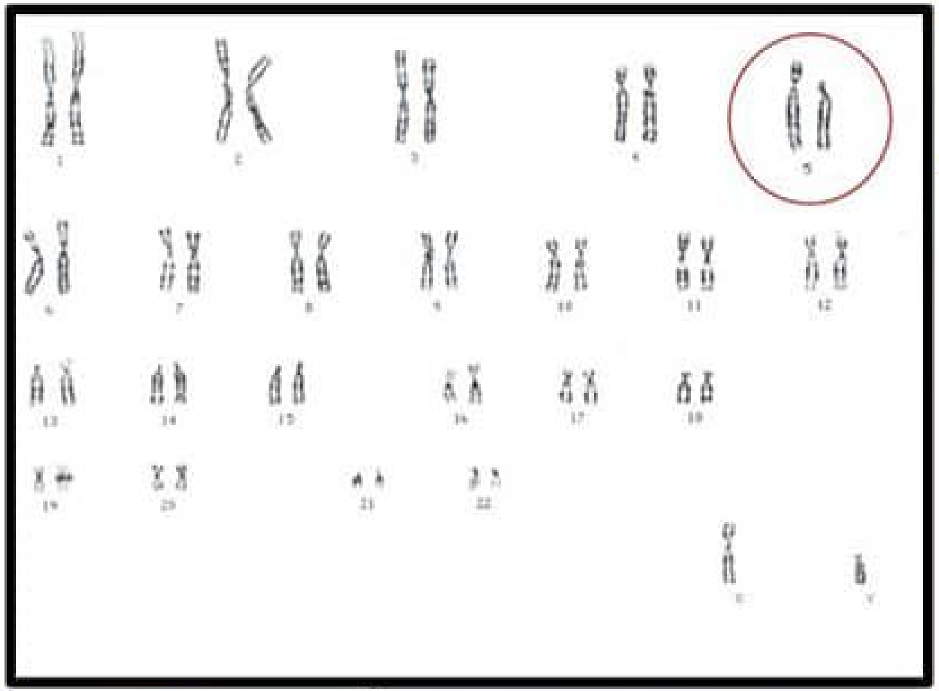
❖ Most common cardiac defect ?

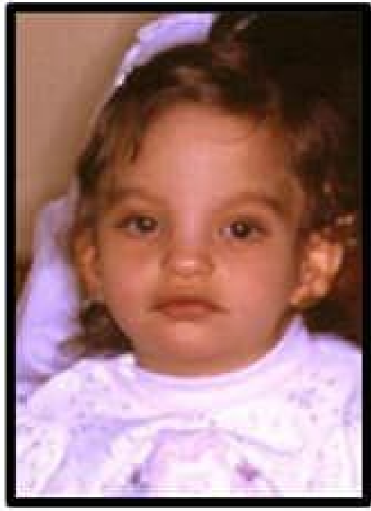
❖ Peripheral pulmonary artery stenosis / pulmonary valve stenosis

❖ Treatment ?

- ✓ Ursodeoxycholic acid (UDCA)
- ✓ Liver transplant

10) Cri du chat syndrome





❖ **Mode of inheritance?**
- ✓ De novo mutation
- ✓ 5p deletion

❖ **Clinical features**
- ✓ **High pitched (Cat's like) cry** (larynx anatomical changes)
- ✓ Moon face with wide spaced eyes
- ✓ Wide and flat nasal bridge
- ✓ Hypotonia
- ✓ Down slanting palpebral fissures
- ✓ Microcephaly
- ✓ Feeding difficulties
- ✓ Intellectual disabilities
- ✓ Failure to thrive

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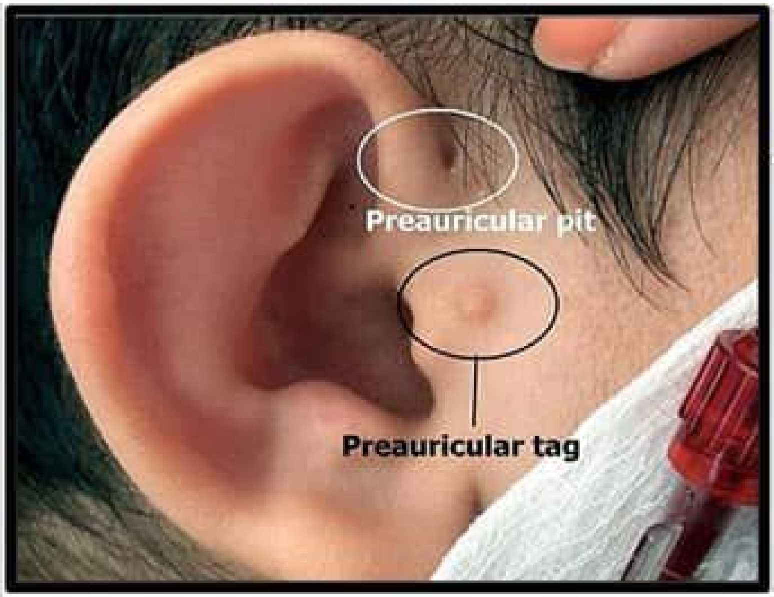
❖ **Common cardiac defect ?**
- ✓ **VSD, ASD, PDA & TOF**

Pediatric On Squares

28) Branchio-oto-renal (BOR) syndrome



Clinical features

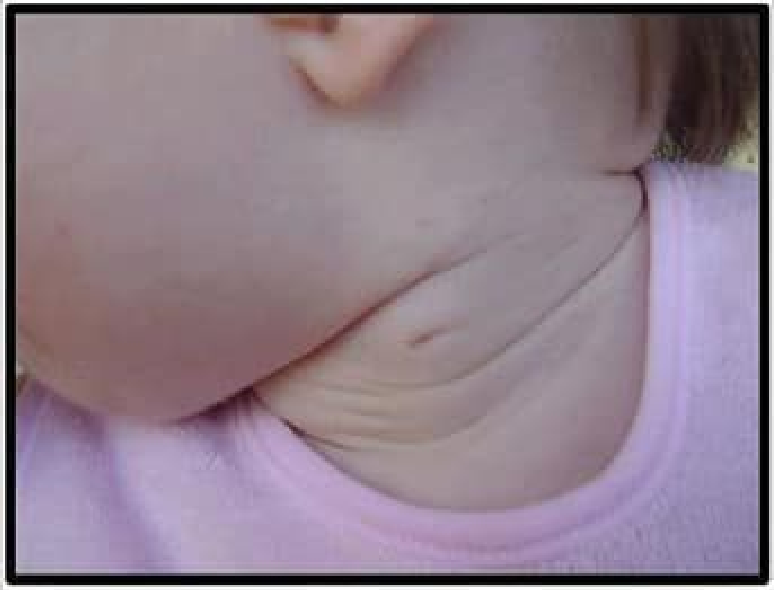
- ✓ Branchial cleft fistulas / cysts
- ✓ Preauricular pits / tags
- ✓ Renal aplasia / hypoplasia
- ✓ Sensory / conductive hearing loss
- ✓ Pulmonary hypoplasia

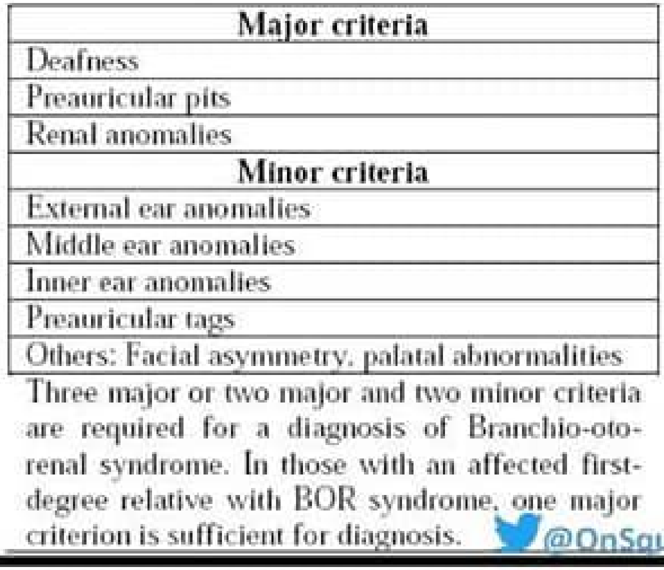
❖ **Mode of inheritance?**

✓ Autosomal dominant

❖ **Laboratory finding ?**

- ✓ Low renin
- ✓ Low aldosterone
- ✓ Hyperkalemia
- ✓ Hyperchloremia
- ✓ Metabolic acidosis





Major criteria
Deafness
Preauricular pits
Renal anomalies
Minor criteria
External ear anomalies
Middle ear anomalies
Inner ear anomalies
Preauricular tags
Others: Facial asymmetry, palatal abnormalities

Three major or two major and two minor criteria are required for a diagnosis of Branchio-oto-renal syndrome. In those with an affected first-degree relative with BOR syndrome, one major criterion is sufficient for diagnosis.

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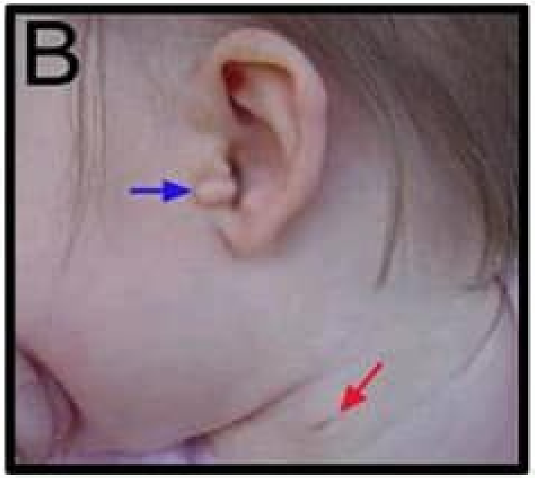

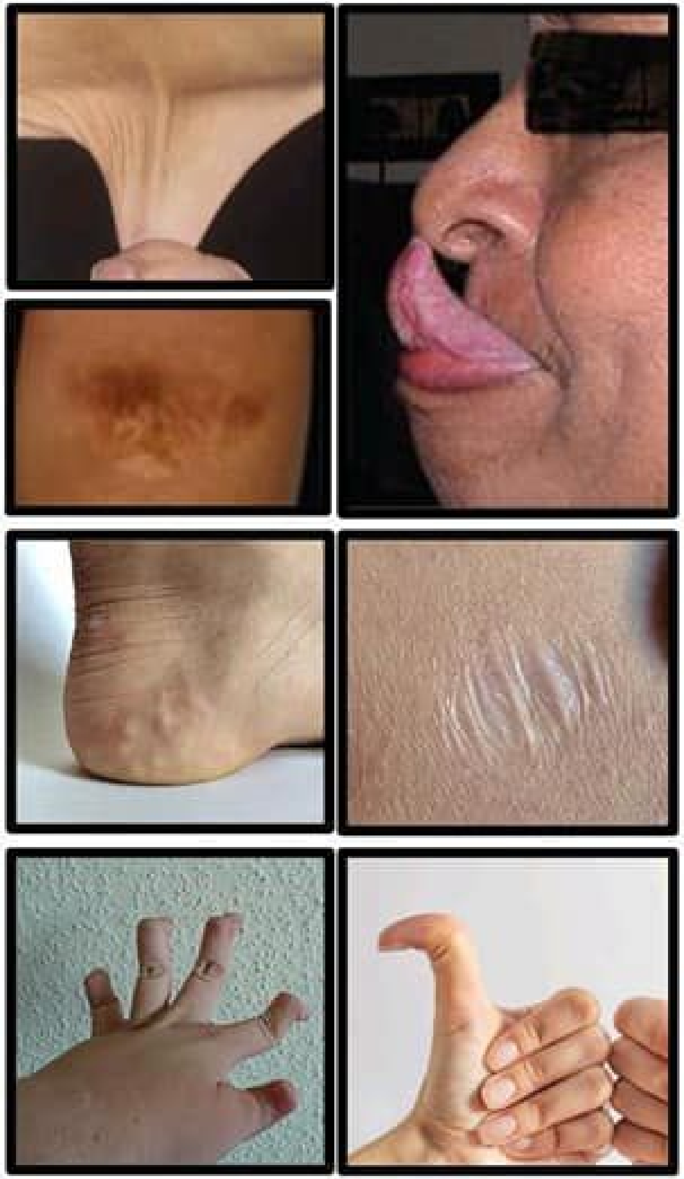

25) Ehlers–Danlos syndromes (EDS)

Clinical features

- ✓ Generalized joint hypermobility
- ✓ Hyperextensible skin
- ✓ Fragile skin.
- ✓ Increased bruising
- ✓ Velvety skin
- ✓ Kyphoscoliosis
- ✓ Swan-neck malformation
- ✓ Piezogenic papules
- ✓ Gorlin's sign
- ✓ Cigarette paper scar
- ✓ Fish mouth appearance of skin tears.
- ✓ Hypotonia

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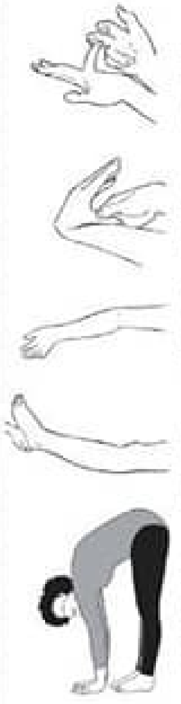
THE BEIGHTON SCORE

How to Assess Joint Hypermobility

A numerical mobility score of 0 to 9, one point allocated for the ability to perform each of the following tests:



Pull little finger back beyond 90°
(one point for each side)

Pull thumb back to touch forearm
(one point for each side)

Bend elbow backwards beyond 10°
(one point for each side)

Bend knee backwards beyond 10°
(one point for each side)

Lie hands flat on floor while keeping knees straight and bending forward at waist

A positive Beighton score for adults is 5 out of the 9 possible points; for children, a positive score is at least 6 out of 9 points.

- ❖ **Mode of inheritance?**
- ✓ Autosomal dominant
- ✓ Rarely AR

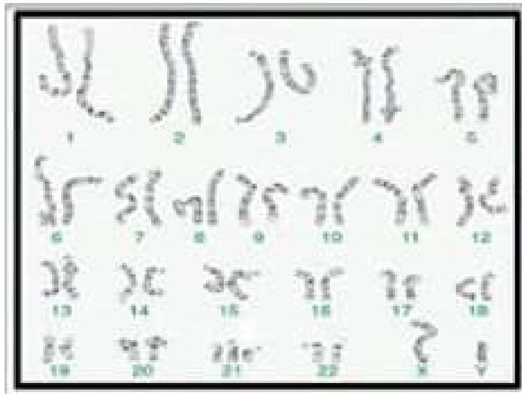
- ❖ **Most common cardiac defect ?**
- ✓ Mitral valve prolapse
- ✓ Aortic root dilatation

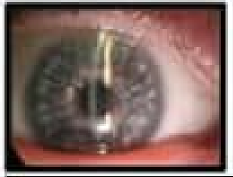
- ❖ **Laboratory finding include normal coagulation expect ?**
- ✓ Capillary fragility test

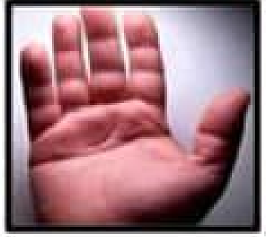
- ❖ **Monitoring?**
- ✓ Annual echocardiogram.

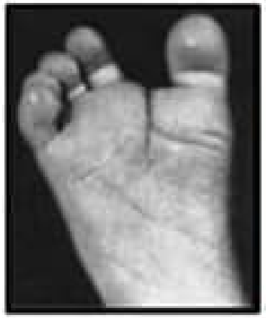
- ❖ **Most severe type?**
- ✓ Vascular (vEDS; EDS type IV)

1) Trisomy 21 (Down syndrome)









Ophthalmology clinical features :

- ✓ Myopia
- ✓ Cataract
- ✓ Glaucoma
- ✓ Brushfield spots (speckled irises)
- ✓ Nystagmus
- ✓ Strabismus

Screen at birth, 6 mo. Than annually

Musculoskeletal clinical features :

- ✓ Short neck, redundant skin
- ✓ Short metacarpals and phalanges
- ✓ Short 5th digit with Clinodactyly
- ✓ Single transverse palmer creases
- ✓ Wide gap between 1st & 2nd toes
- ✓ Short sternum
- ✓ Atlantoaxial instability (screen each visit)
- ✓ Hip dysplasia
- ✓ Recurrent joints dislocation

Cardiac clinical finding:

- ✓ Endocardial cushing defect (AVSD) **(MOST COMMON)**
- ✓ Ventricular septal defect
- ✓ Atrial septal defect
- ✓ Patent ductus arteriosus
- ✓ Pulmonary hypertension

Screen at birth

Facial clinical features :

- ✓ Brachycephaly
- ✓ Up slanted palpebral fissures
- ✓ Epicanthal folds
- ✓ Three fontanels
- ✓ Flat nasal bridge , small nose
- ✓ Short hard palate
- ✓ Microcephaly
- ✓ Low set ears
- ✓ Hearing loss
- ✓ Recurrent otitis media

Hearing screen Screen at birth than annually

Hematological finding:

- ✓ Transient myeloproliferative dis.
- ✓ ALL (> 1y.o)
- ✓ AML (< 1y.o)

Screen at birth

Endocrine finding:

- ✓ **Hypothyroidism**
- ✓ Hyperthyroidism
- ✓ Diabetes mellitus
- ✓ Infertility
- ✓ Obesity

Screen at birth, 6 mo. than annually

Respiratory finding:

- ✓ Obstructive sleep apnea
- ✓ Recurrent infections

Screen at 1 Y.O

Neuropsychiatric finding:

- ✓ **Hypotonia**
- ✓ Developmental delay
- ✓ Autism
- ✓ Seizure

Screen each visit

Gastrointestinal finding:

- ✓ Duodenal atresia
- ✓ Annular pancreas
- ✓ Tracheoesophageal fistula
- ✓ Hirschsprung disease
- ✓ Imperforated anus
- ✓ Neonatal cholestasis
- ✓ Celiac disease (Screen at 2y.o)

Causes:

- ✓ Nondisjunction (95%)
- ✓ Translocation (4%)
- ✓ Mosaic (1%)

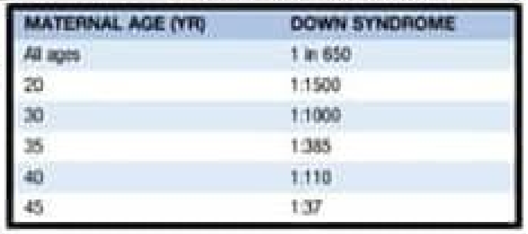
Recurrence 1%

When the recurrence become 100%?

- ✓ If a parent has 21:21 translocation

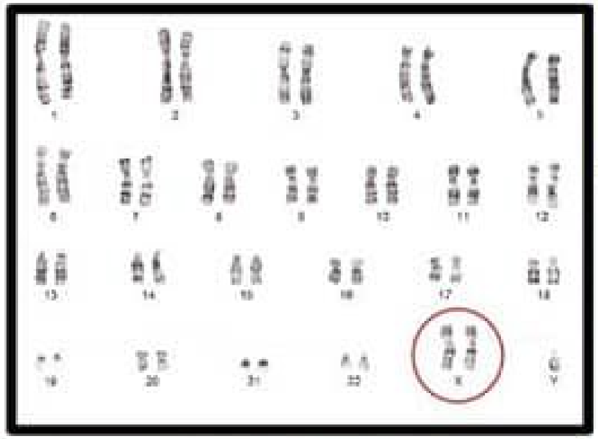
Prenatal screen lab finding?

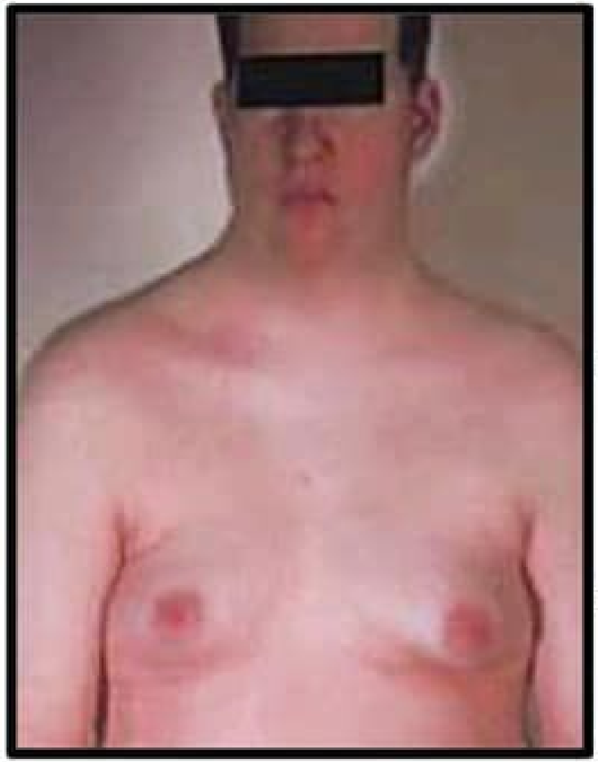
- ✓ Low α feto protein
- ✓ Low estriol
- ✓ High hCG and high inhibin



MATERNAL AGE (YR)	DOWN SYNDROME
All ages	1 in 650
20	1:1500
30	1:1000
35	1:385
40	1:110
45	1:37

6) Klinefelter Syndrome XXY

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❖ Clinical features

- ✓ **Gynecomastia**
- ✓ Tall stature
- ✓ **Small testes**
- ✓ Micropenis
- ✓ Normal pubic and axillary hair
- ✓ Intellectual disability
- ✓ Infertility
- ✓ Behavioral problems

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The most common cause of primary hypogonadism and infertility in males

Recurrence rate 1 – 2 %

❖ Laboratory finding ?

- ✓ Low testosterone
- ✓ High FSH/LH

❖ Increases risk of :

- ✓ Pulmonary disease
- ✓ Varicose vain
- ✓ ADHD

❖ Increases risk of which Malignancies ?

- ✓ Breast cancer
- ✓ Testicular cancer

❖ What is the most effective treatment ?

- ✓ Testosterone replacement therapy

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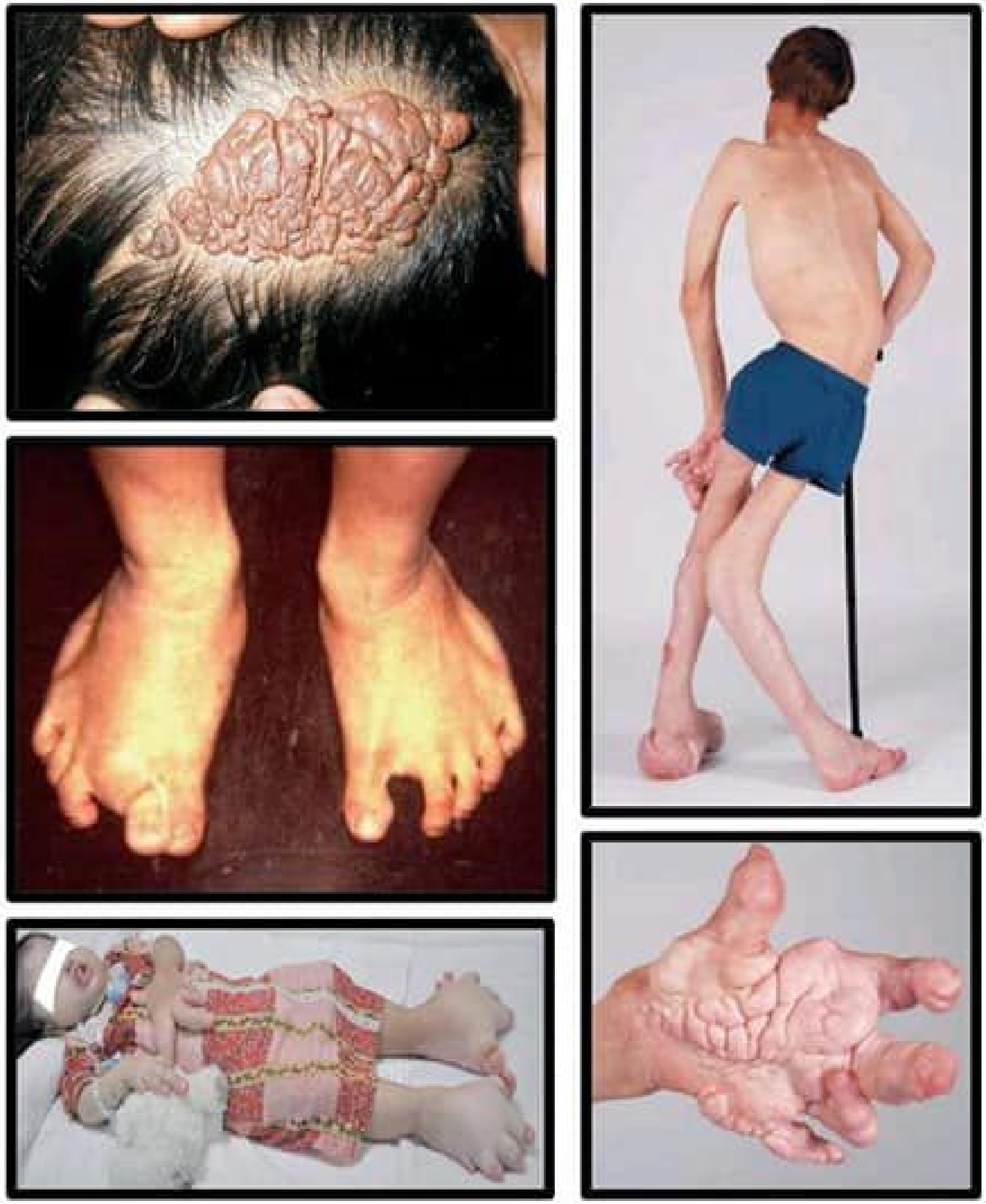

19) Proteus Syndrome

- **Clinical features**
  - ✓ Macrodactyly
  - ✓ Hemihypertrophy
  - ✓ Skin changes (lipomas, vascular malformations, connective tissue nevi, epidermal)
  - ✓ Scoliosis
  - ✓ Tissue hypertrophy
  - ✓ Accelerated growth
  - ✓ Developmental delay
  - ✓ Increase risk of malignancies

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- **What is Pathagnomic feature of Proteus syndrome ?**
  - ✓ Connective tissue nevi, mainly "Cerebriform nevi"

- **Mode of inheritance?**
  - ✓ Sporadic

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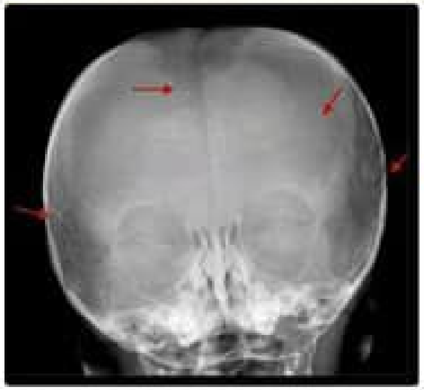
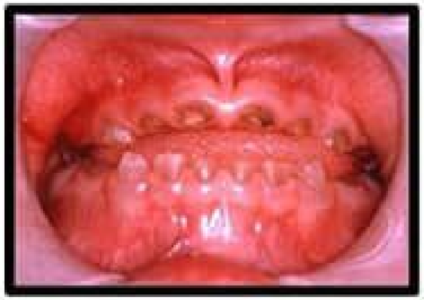
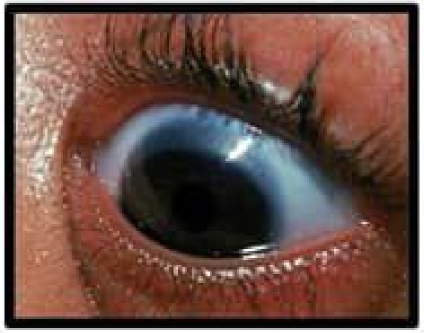
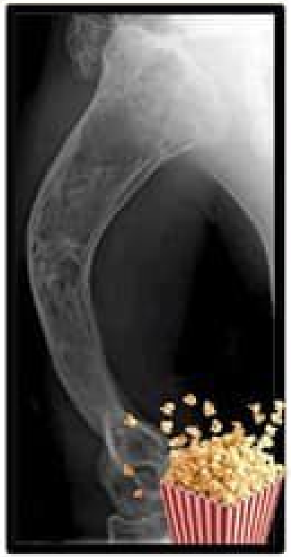
- **Increases risk of which Malignancies ?**
  - ✓ Embryonic tumor

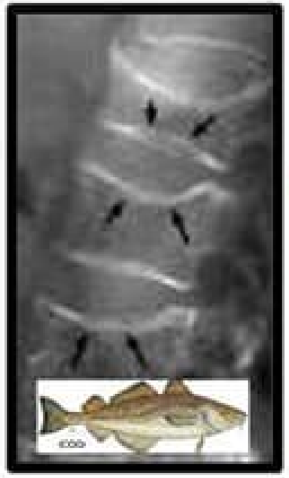
23) Osteogenesis Imperfecta











Clinical features

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- Short stature
- Scoliosis
- Blue sclera
- Dentinogenesis imperfecta
- Hyperextensible joints
- Easy bruising.
- Wormian bones (small, irregular bones along the cranial sutures)
- Codfish vertebrae
- Flared metaphysis (popcorn-like)

❖ Mode of inheritance?

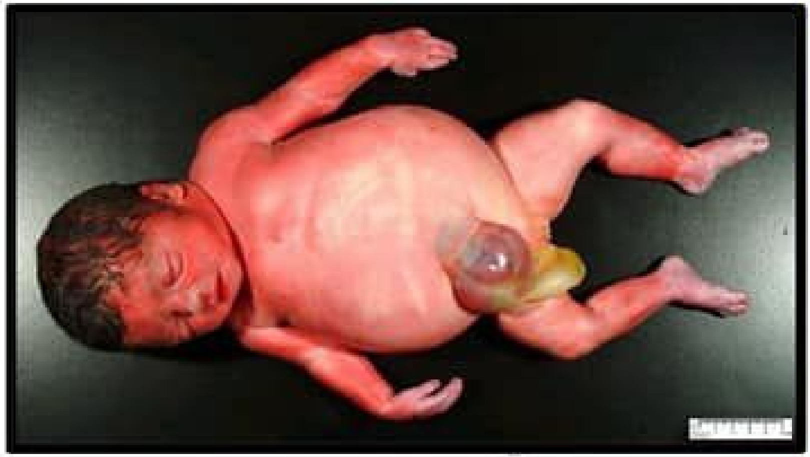
- ✓ AD (I – IV)
- ✓ AR (rare types + IIB)
- ✓ COL1A1 gene

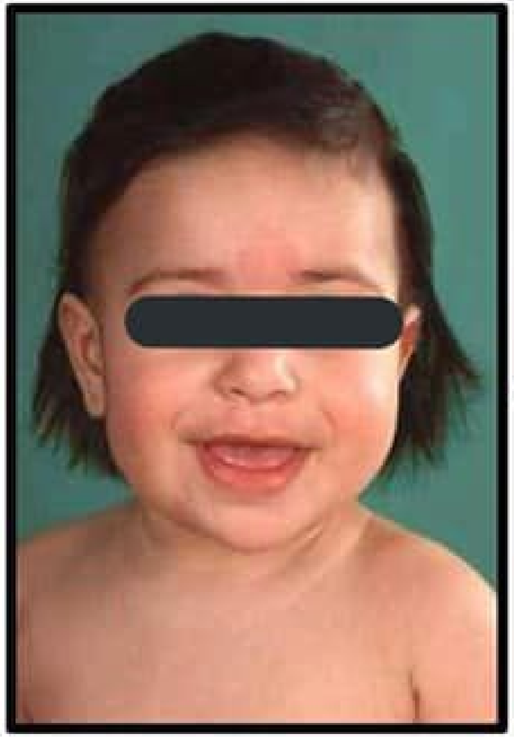
❖ Common Types

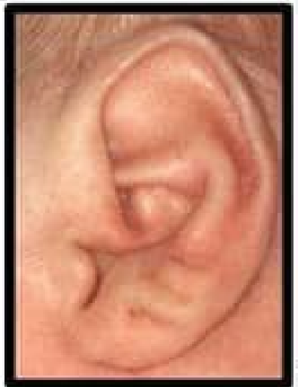
1. Type I
   - Most common
   - Mildest form
   - Classic nondeforming
   - Hearing loss in 50%
2. Type II
   - Most severe
   - Death during newborn
3. Type III
   - Progressive deforming
   - Hydrocephalus
4. Type IV
   - Normal sclera
   - Tibial bowing (hallmark)

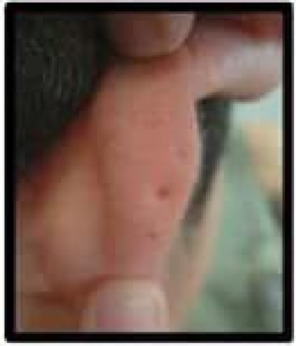
❖ Laboratory finding ?

- ✓ High alkaline phosphatase
- ✓ Hypercalciuria









16) Beckwith-Wiedemann syndrome

❖ Clinical features

- ✓ Large for gestational age
- ✓ Macroglossia
- ✓ Omphalocele
- ✓ **Ear lobe creases**
- ✓ **Posterior auricular pits**
- ✓ Hemihypertrophy
- ✓ Cryptorchidism
- ✓ Umbilical hernia
- ✓ Normal intelligence

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❖ Laboratory finding ?

- ✓ Hypoglycemia
- ✓ Hyperinsulinism
  - ➢ Due pancreatic islet hyperplasia

❖ Mode of inheritance?

- ✓ Sporadic
- ✓ Autosomal dominant
- ✓ 15q11 deletion

❖ Increases risk of which Malignancies ?

- ✓ Wilms tumor
- ✓ Hepatoblastoma

❖ Clinic follow up ?

- ✓ **Abdominal US**
  - Q3 months until 4 Y.O
- ✓ **Alpha fetoprotein**
  - Q3 months until 4 Y.O
- ✓ **Renal US**
  - Q3 months from 4-7 Y.O

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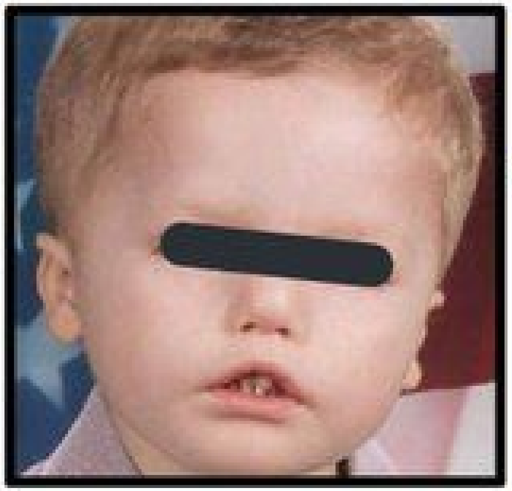
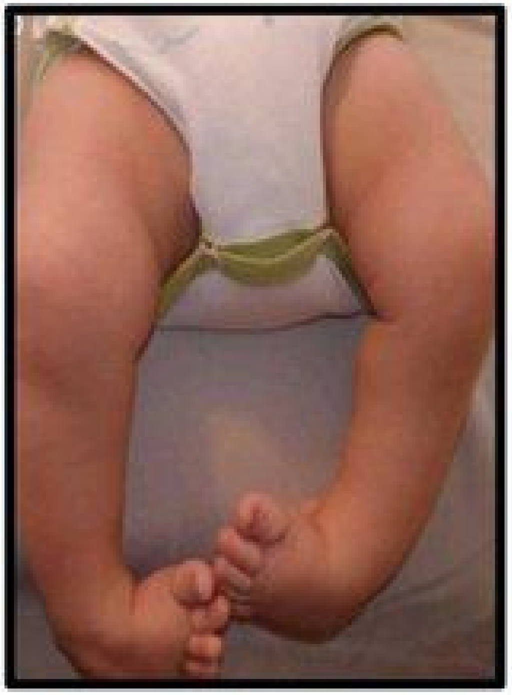
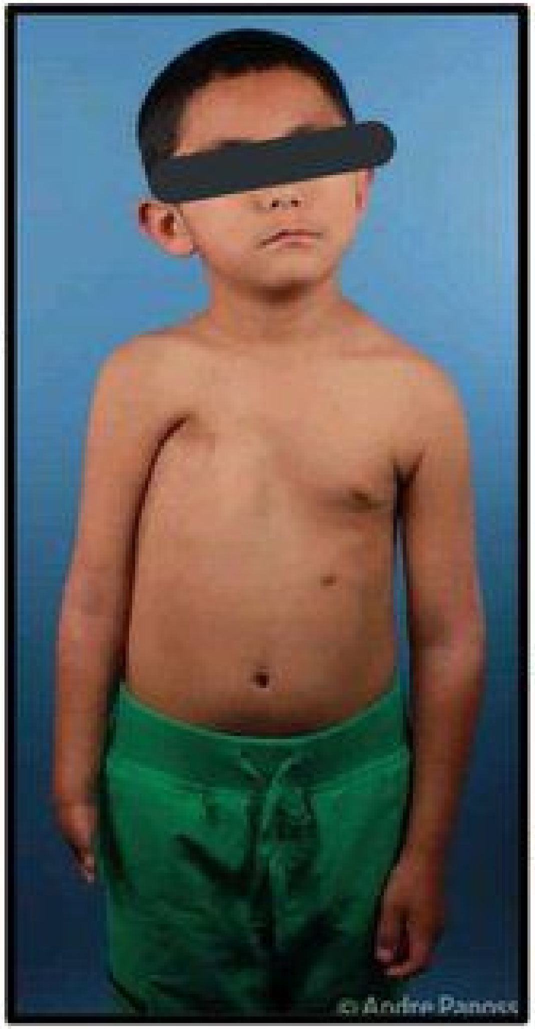
46) Möbius Syndrome







- **Clinical features**
  - ✓ Facial (VII) nerve paralysis
  - ✓ Abducens (VI) nerve paralysis
  - ✓ Expressionless
  - ✓ Strabismus
  - ✓ Club feet
  - ✓ Absent fingers or toes
  - ✓ Unilateral chest deformity
  - ✓ Tongue atrophy
  - ✓ Dental problems

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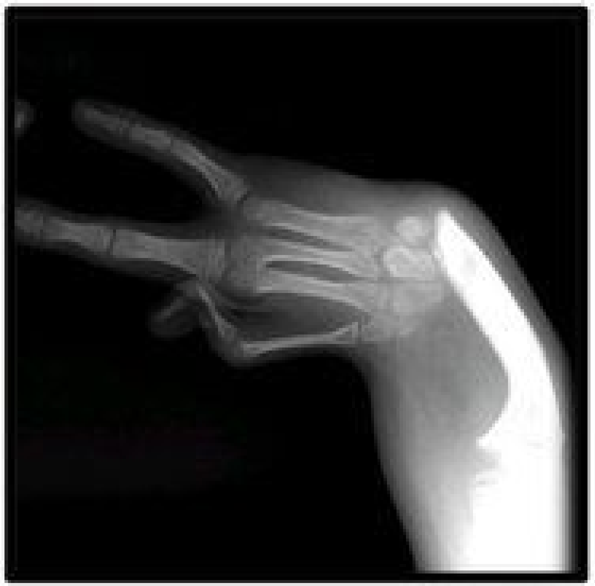
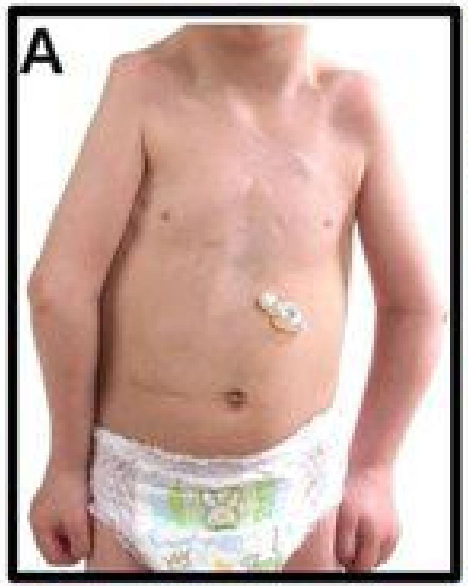
- **Mode of inheritance?**
  - ✓ Autosomal dominant

- **Strong association with which syndrome ?**
  - ✓ Poland Syndrome

47) Holt Oram Syndrome





- **Clinical features**
  - ✓ Thumb
    - Aplasia / hypoplasia
    - Triphalangeal
  - ✓ Radial hypoplasia
  - ✓ Clavicle hypoplasia

Pediatric On Squares
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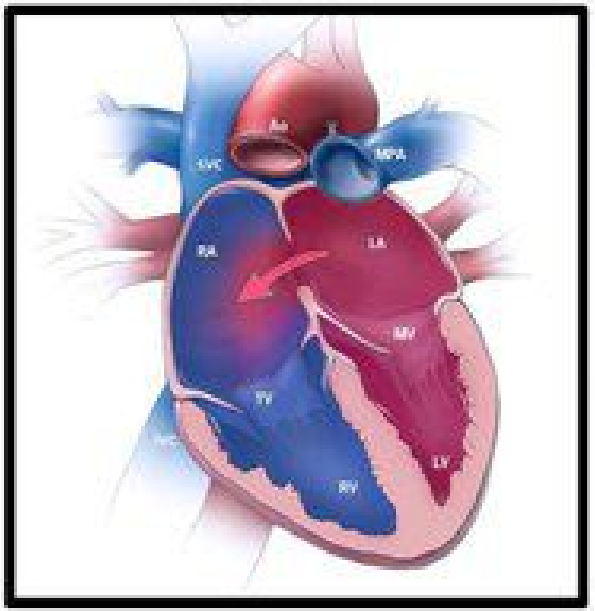
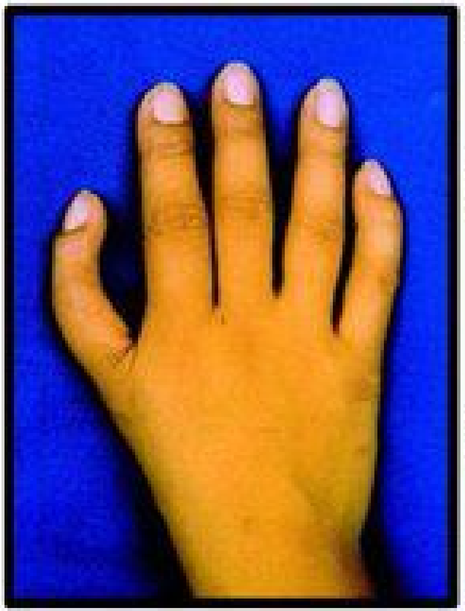
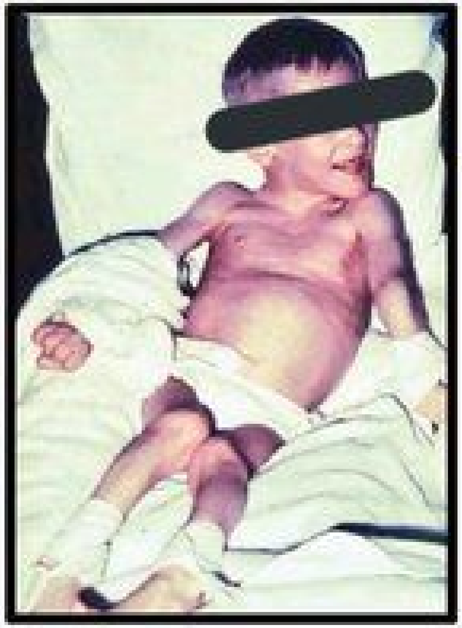


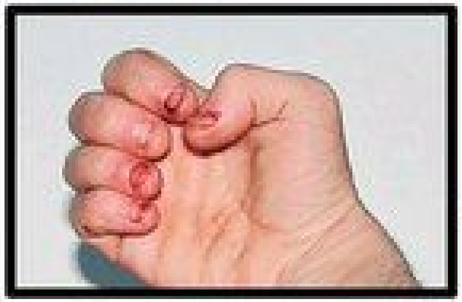


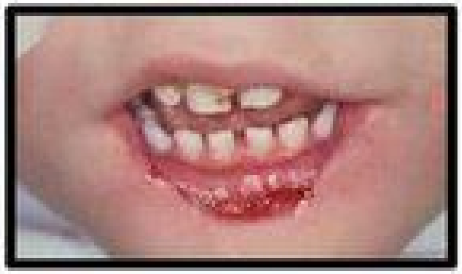
- **Mode of inheritance?**
  - ✓ Autosomal dominant

- **What is the most common cardiac defect?**
  - ✓ Atrial septal defect (ASD)
  - ✓ 1st degree heart block

NO hematological abnormalities







48) Lesch Nyhan Syndrome

❖ Clinical features

- ✓ Self-injury (Most distinctive behavioral problem)
  - Fingers & mouth biting
  - Head banging
- ✓ Dystonia
- ✓ Chorea
- ✓ Hypotonia
- ✓ Ballismus
- ✓ Developmental delay

Pediatric On Squares

❖ Mode of inheritance?

- ✓ X-linked recessive
- ✓ HPRT1 gene
- ✓ Defect in purine metabolism

❖ Laboratory finding ?

- ✓ Hyperuricemia

❖ Complications :

- ✓ Gouty arthritis
- ✓ Kidney & bladder stones
- ✓ Renal failure

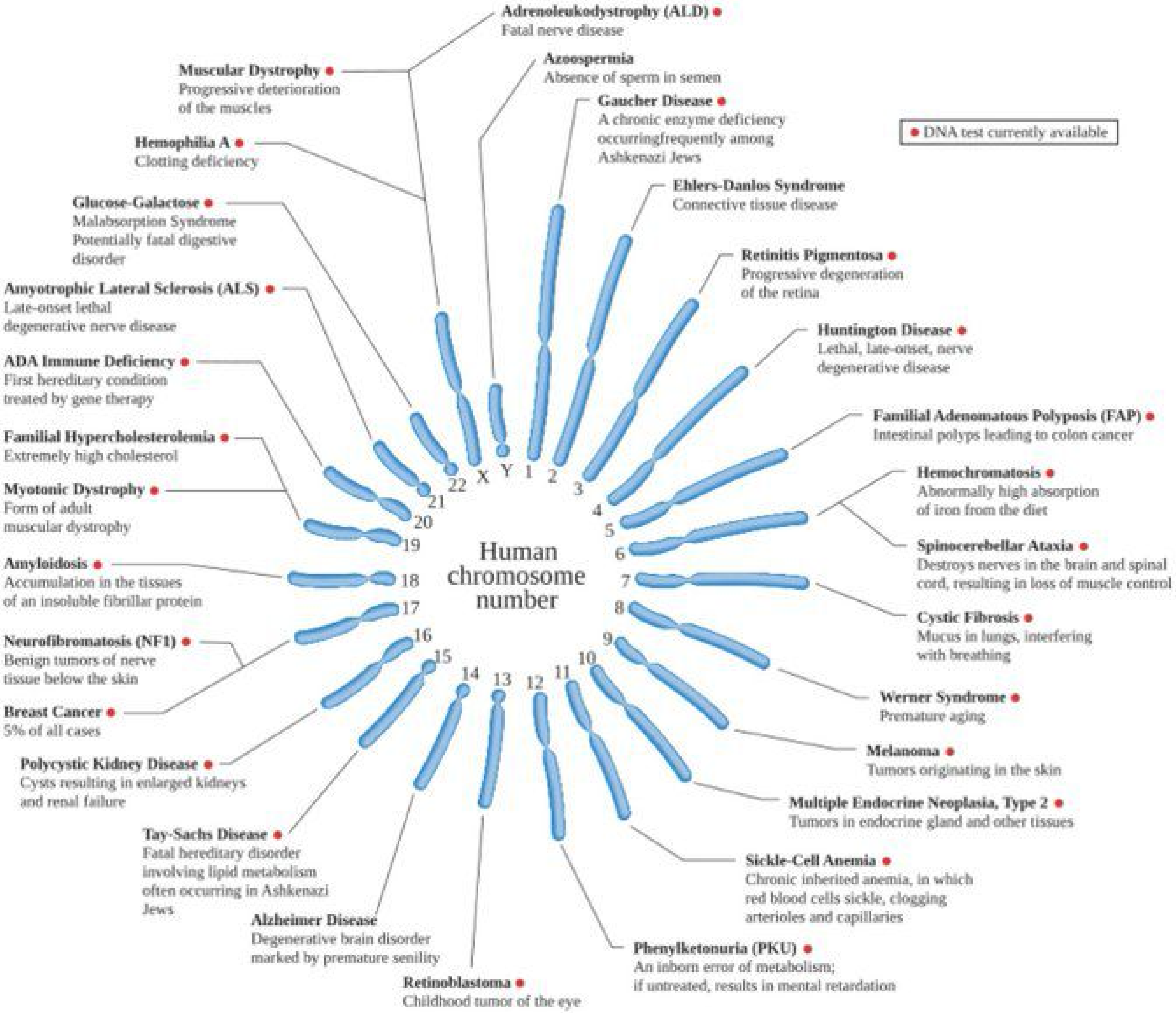
❖ Most common cause of death?

- ✓ Renal failure

❖ Treatment :

@OnSquares

- ✓ Allopurinol
- ✓ High fluid intake
- ✓ Behavioral therapy


Human chromosome number
● DNA test currently available
Adrenoleukodystrophy (ALD) ●
Fatal nerve disease
Azoospermia
Absence of sperm in semen
Gaucher Disease ●
A chronic enzyme deficiency occurringfrequently among Ashkenazi Jews
Ehlers-Danlos Syndrome
Connective tissue disease
Retinitis Pigmentosa ●
Progressive degeneration of the retina
Huntington Disease ●
Lethal, late-onset, nerve degenerative disease
Familial Adenomatous Polyposis (FAP) ●
Intestinal polyps leading to colon cancer
Hemochromatosis ●
Abnormally high absorption of iron from the diet
Spinocerebellar Ataxia ●
Destroys nerves in the brain and spinal cord, resulting in loss of muscle control
Cystic Fibrosis ●
Mucus in lungs, interfering with breathing
Werner Syndrome ●
Premature aging
Melanoma ●
Tumors originating in the skin
Multiple Endocrine Neoplasia, Type 2 ●
Tumors in endocrine gland and other tissues
Sickle-Cell Anemia ●
Chronic inherited anemia, in which red blood cells sickle, clogging arterioles and capillaries
Phenylketonuria (PKU) ●
An inborn error of metabolism; if untreated, results in mental retardation
Retinoblastoma ●
Childhood tumor of the eye
Alzheimer Disease
Degenerative brain disorder marked by premature senility
Tay-Sachs Disease ●
Fatal hereditary disorder involving lipid metabolism often occurring in Ashkenazi Jews
Polycystic Kidney Disease ●
Cysts resulting in enlarged kidneys and renal failure
Breast Cancer ●
5% of all cases
Neurofibromatosis (NF1) ●
Benign tumors of nerve tissue below the skin
Amyloidosis ●
Accumulation in the tissues of an insoluble fibrillar protein
Myotonic Dystrophy ●
Form of adult muscular dystrophy
Familial Hypercholesterolemia ●
Extremely high cholesterol
ADA Immune Deficiency ●
First hereditary condition treated by gene therapy
Amyotrophic Lateral Sclerosis (ALS) ●
Late-onset lethal degenerative nerve disease
Glucose-Galactose ●
Malabsorption Syndrome
Potentially fatal digestive disorder
Hemophilia A ●
Clotting deficiency
Muscular Dystrophy ●
Progressive deterioration of the muscles
X
Y
1
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22

Shwachman-Diamond syndrome (SDS)

@OnSquares

- **Mode of inheritance**
  - ✓ Autosomal recessive
  - ✓ SBDS gene

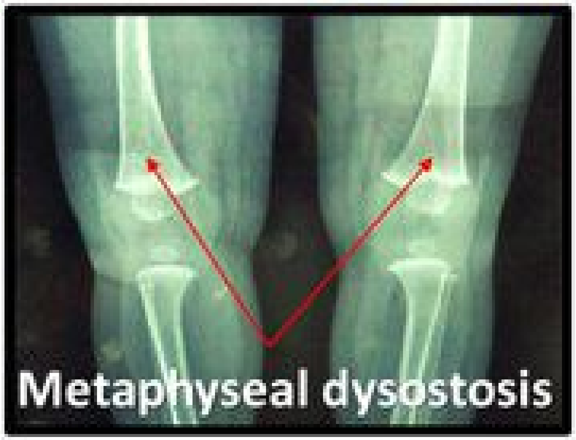
- **Clinical features:**
  - ✓ FTT
  - ✓ Steatorrhea
  - ✓ Recurrent infection
  - ✓ Short stature
  - ✓ Metaphyseal dysostosis
  - ✓ Dipper rash

2nd most common cause of exocrine pancreatic insufficiency.

- Laboratory findings:
  - ✓ Neutropenia
  - ✓ Anemia & thrombocytopenia
  - ✓ Low pancreatic trypsinogen
  - ✓ Low fecal elastase
  - ✓ High HgF
  - ✓ Fat-soluble vitamin deficiency

- **Increase risk for developing :**
  - ✓ Acute myeloid leukemia (AML)
  - ✓ Myelodysplastic syndromes (MDS)

- **Treatment :**
  - ✓ Pancreatic enzymes replacement.
  - ✓ Granulocyte colony-stimulating factor (G-CSF).



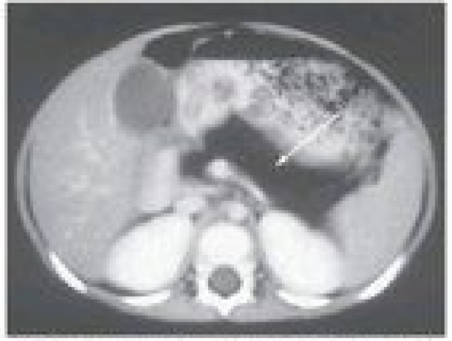
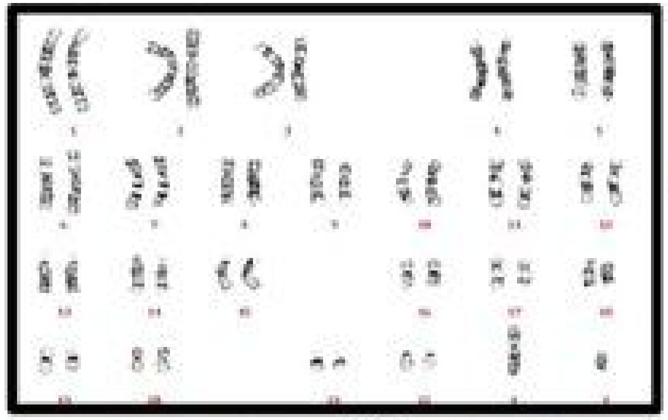
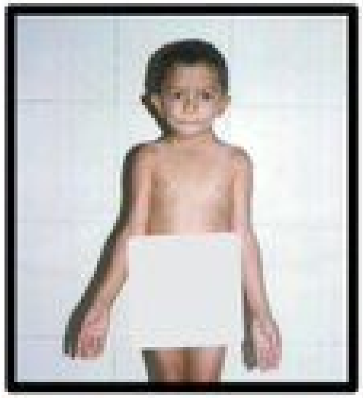
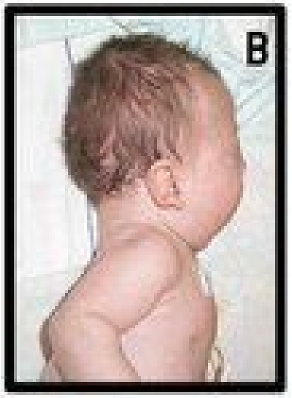
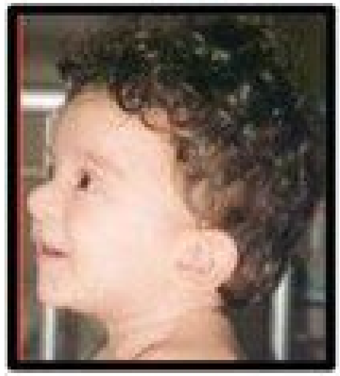


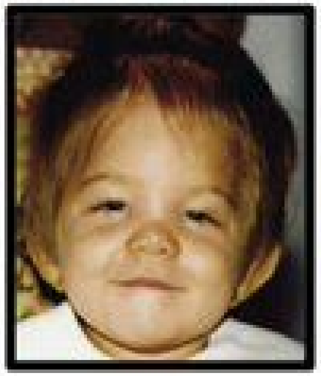
Fig. 376.1 CT appearance of the pancreas in a patient with Shwachman-Diamond syndrome. Note that the pancreas (arrow) retains a typical size and shape, but it is highly fatty and therefore appears as a very low-density structure. (Courtesy Prof. Peter Durie, Hospital for Sick Children, Toronto, Ontario.)











5) Noonan Syndrome

❖ **Clinical features**

- ✓ **Down slanting palpebral fissures**
- ✓ Short stature
- ✓ Shield chest
- ✓ Cubitus valgus
- ✓ Low posterior hairline
- ✓ Webbed neck
- ✓ Posterior rotated ears
- ✓ Cryptorchidism
- ✓ Intellectual disability
- ✓ Delayed puberty
- ✓ Ptosis

Pediatric On Squares

❖ **Mode of inheritance?**

- ✓ Autosomal dominant
- ✓ PTPN11 gene on 12q24
- ✓ Normal karyotype

❖ **What is the most common cardiac defect?**

1. Pulmonary stenosis
2. Hypertrophic cardiomyopathy

❖ **Labs finding ?**

- ✓ Clotting factor deficiencies
  - Mainly factor XI & XII
- ✓ Abnormal platelet count/function

❖ **Increases risk of which Malignancy ?**

- ✓ Acute lymphocytic leukemia (ALL)
- ✓ Chronic myeloid leukemia (CML)

❖ **Treatment**

- ✓ Growth hormone

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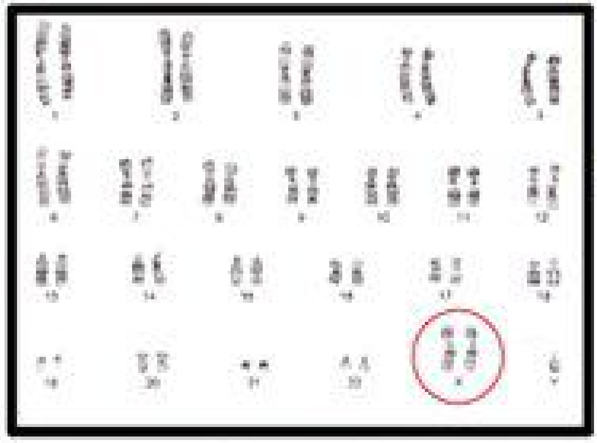

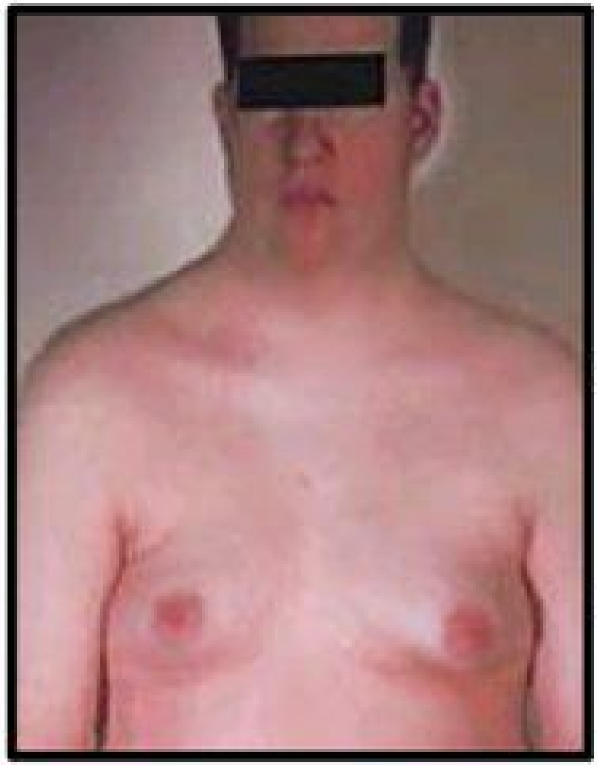

6) Klinefelter Syndrome XXY

❖ **Clinical features**

- ✓ **Gynecomastia**
- ✓ Tall stature
- ✓ **Small testes**
- ✓ Micropenis
- ✓ Normal pubic and axillary hair
- ✓ Intellectual disability
- ✓ Infertility
- ✓ Behavioral problems

Pediatric On Squares

The most common cause of primary hypogonadism and infertility in males

Recurrence rate 1 – 2 %

❖ **Laboratory finding ?**

- ✓ Low testosterone
- ✓ High FSH/LH

❖ **Increases risk of :**

- ✓ Pulmonary disease
- ✓ Varicose vain
- ✓ ADHD

❖ **Increases risk of which Malignancies ?**

- ✓ Breast cancer
- ✓ Testicular cancer

❖ **What is the most effective treatment ?**

- ✓ Testosterone replacement therapy

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AICARDI syndrome has

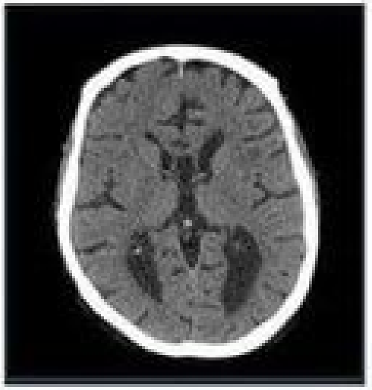
Triad of CARDI

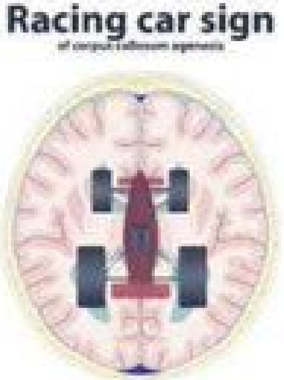
Corpus callosum Agenesis

Retinal Defects
(circumscribed pits or lacunae)

Infantile spasm

& Racing CAR sign is seen in CT





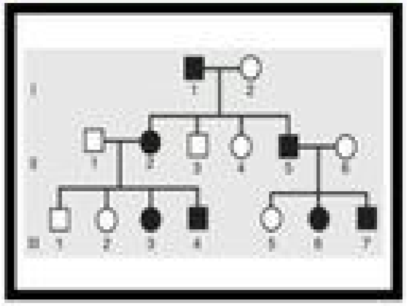
Racing car sign

also they are RAC
(Resistant to Anti Convulsants)

Mediwood
by Dr Naveen Koval

Mediwood

How to Read a Pedigree Chart ?

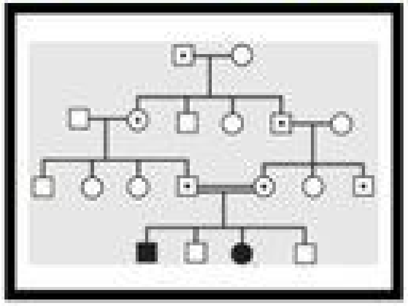


Autosomal dominant

- Both sex equally affected
- Both sexes transmit to offspring
- No skipped generation
- Every child has a parent with disorder

Most common examples

- **Achondroplasia**
- **Von Willebrand disease**
- **Marfan syndrome**
- **Alagille syndrome**
- **Neurofibromatosis 1&2**
- **Myotonic dystrophy**
- **William syndrome**

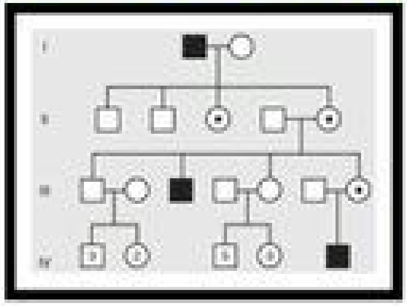


Autosomal recessive

- Both sex equally affected
- Both sexes transmit to offspring
- Skipped generation, or
- No prior family history

Most common examples

- **Sickle cell anemia**
- **Beta thalassemia**
- **Cystic fibrosis**
- **Factor 13 deficiency**
- **Fanconi anemia**
- **TAR syndrome**
- **Phenylketonuria**

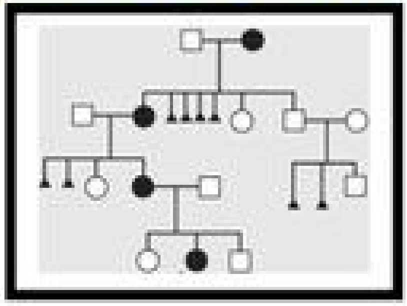


X-linked recessive

- Males much more frequently affected than females
- No father to sun transmission
- Skipped generation

Most common examples

- **Hemophilia A**
- **Hemophilia B**
- **G6PD**
- **Duchenne muscular dystrophy**
- **Lech Nyhan syndrome**
- **OTC deficiency**

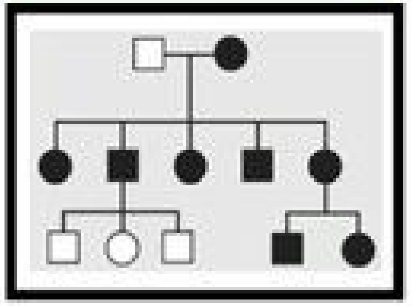


X-linked dominant

- Female twice likely to be affected
- No father to sun transmission
- Affected male 100% transmit it to daughters

Most common examples

- **Hypophosphatemic rickets**
- **Incontinentia pigmenti**
- **Fragile X syndrome**
- **Rett syndrome**
- **Aicardi syndrome**
- **Alport syndrome**
- **Goltz syndrome**



Mitochondrial

- Both sex equally affected
- Only female can transmit the disease
- Affected males never transmit the disease, but females 100% transmit

Most common examples

- **MELAS**
- **MERFF**
- **NARP**
- **Kearns Sayer syndrome**
- **Leigh syndrome**
- **Pearson syndrome**

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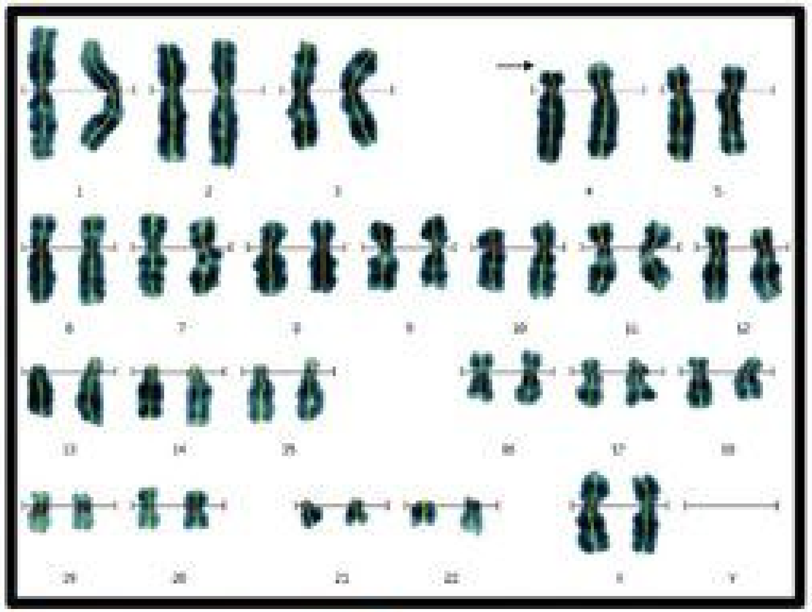
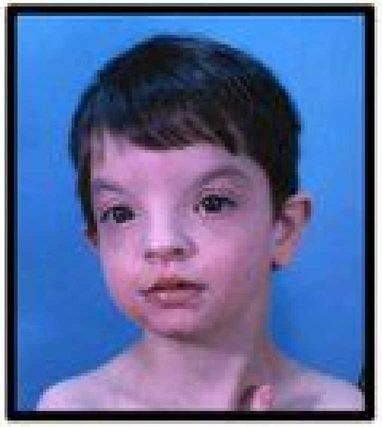
11) Wolf–Hirschhorn syndrome





❖ Clinical features:

- ✓ Microcephaly
- ✓ Hypertelorism
- ✓ Prominent glabella
- ✓ Frontal bossing
- ✓ **Greek helmet face**
- ✓ Beaked nose
- ✓ Hypotonia
- ✓ Seizures
- ✓ Cardiac defect

Pediatric On Squares

❖ Mode of inheritance?

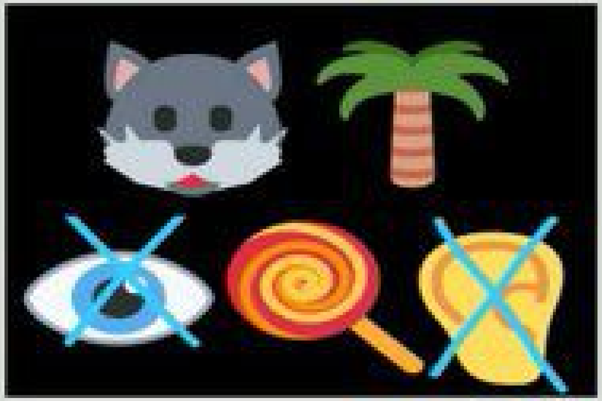
- ✓ De novo
- ✓ Deletion of the short arm of chromosome 4

❖ Laboratory finding ?

- ✓ IgA deficiency

≠

Wolf–Farm syndrome



❖ Clinical features:

- ✓ Diabetes insipidus
- ✓ Diabetes mellitus
- ✓ Blindness
- ✓ Deafness

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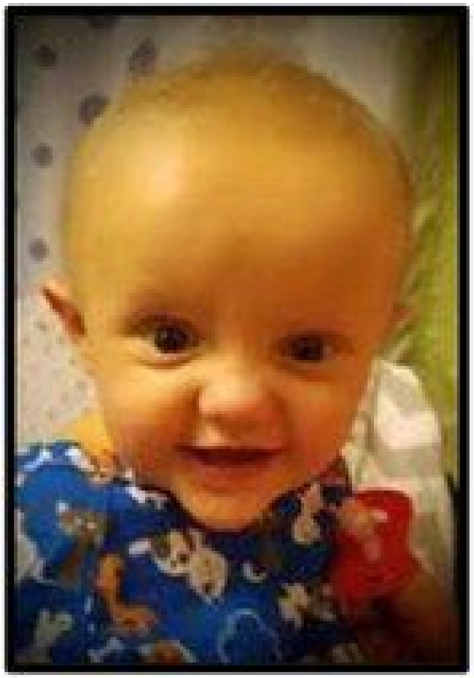
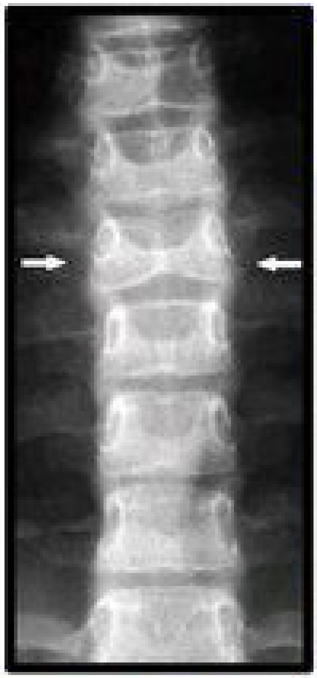
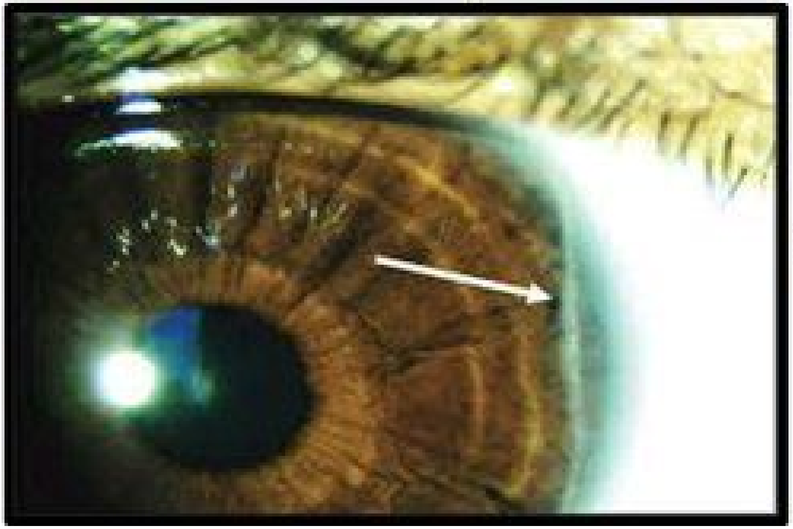






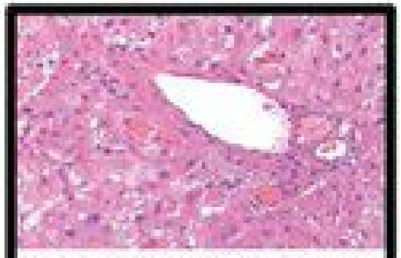
9) Alagille syndrome

- **Clinical features**
  - ✓ **Triangular face with pointed chin**
  - ✓ Long nose
  - ✓ Cholestatic jaundice
  - ✓ **Posterior embryotoxon**
  - ✓ **Butterfly vertebrae**

Liver biopsy show

↓

Paucity of bile duct



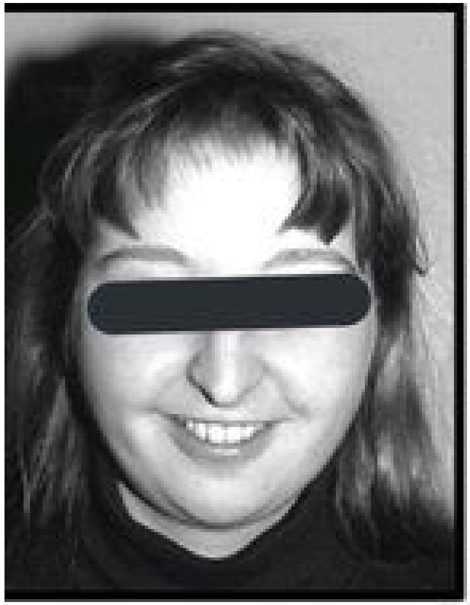
- **Mode of inheritance?**
  - ✓ Autosomal dominant
  - ✓ 20p12 deletion
  - ✓ JAG1 gene

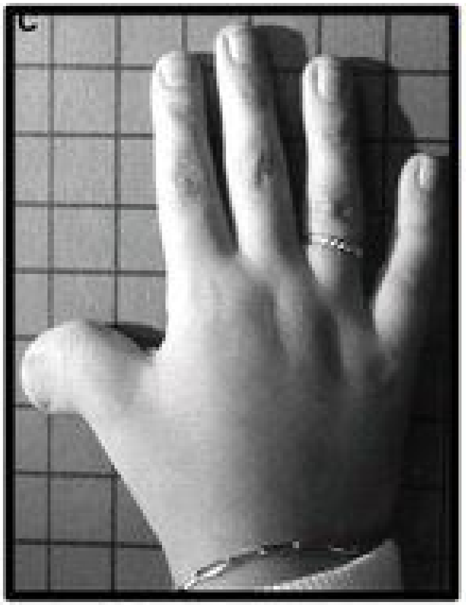
Pediatric On Squares

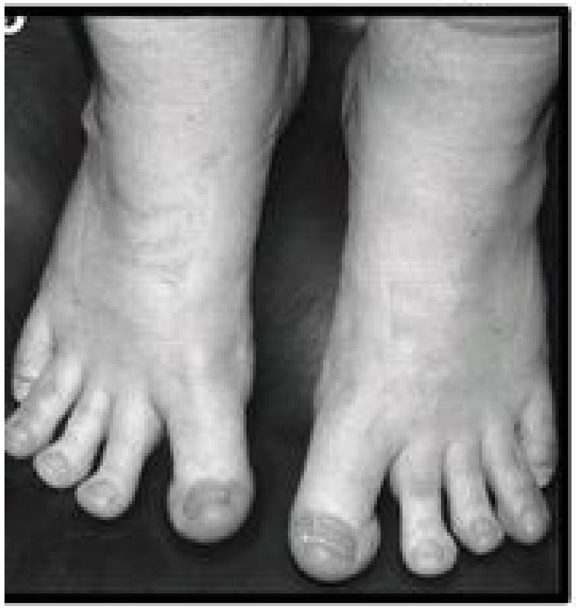
@OnSquares

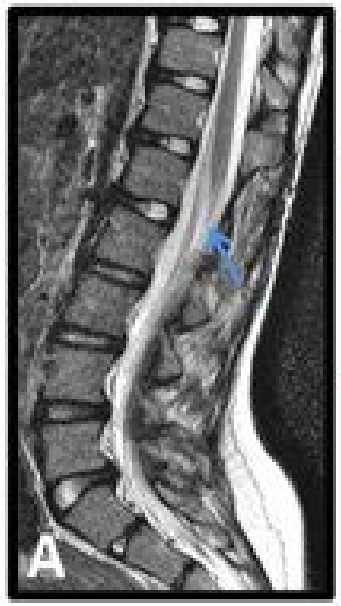
- **Most common cardiac defect ?**
- Peripheral pulmonary artery stenosis / pulmonary valve stenosis

- Treatment ?
  - ✓ Ursodeoxycholic acid (UDCA)
  - ✓ Liver transplant









12) Rubinstein Taybi Syndrome

Clinical features

- ✓ **Broad thumbs and great toes**
- ✓ **Prominent nasal septum , beaked nose**
- ✓ Microcephaly
- ✓ Large nails
- ✓ Long eyelashes
- ✓ Spinal cord tethering
- ✓ Cardiac defect
- ✓ Growth & mental retardation

Pediatric On Squares
@OnSquares

Mode of inheritance?

- ✓ Autosomal dominant
- ✓ Microdeletion 16q

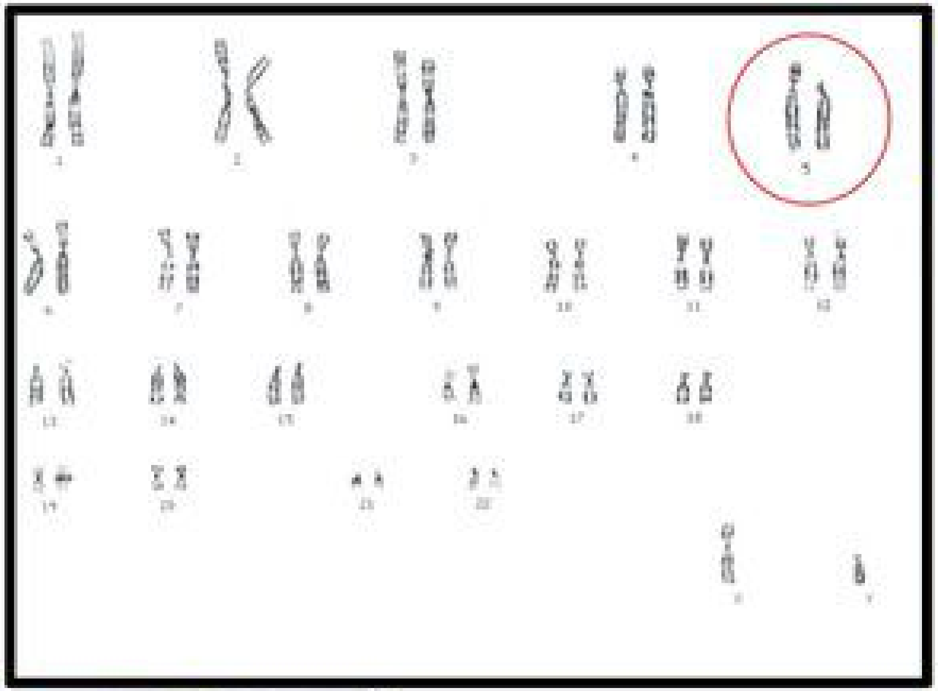
What is the most common cardiac defect?

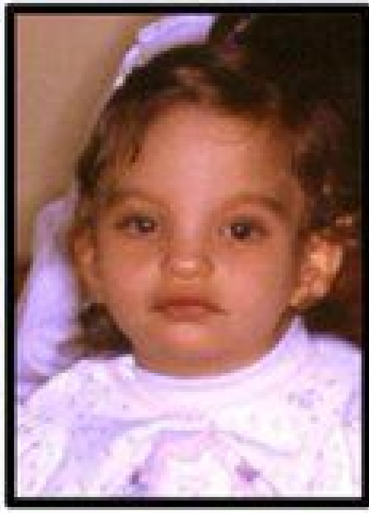
- ✓ Ventricular septal defect (VSD)

⚠ **CAUTION !!**

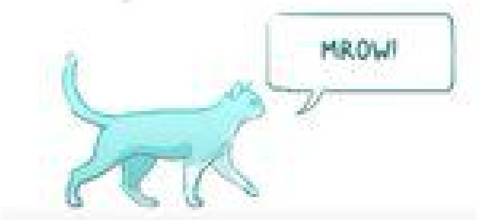
Rubinstein taybi syndrome have an increase risk of complications from anesthesia

10) Cri du chat syndrome





❖ **Mode of inheritance?**
- ✓ De novo mutation
- ✓ 5p deletion



❖ **Clinical features**
- ✓ **High pitched (Cat's like) cry** (larynx anatomical changes)
- ✓ Moon face with wide spaced eyes
- ✓ Wide and flat nasal bridge
- ✓ Hypotonia
- ✓ Down slanting palpebral fissures
- ✓ Microcephaly
- ✓ Feeding difficulties
- ✓ Intellectual disabilities
- ✓ Failure to thrive

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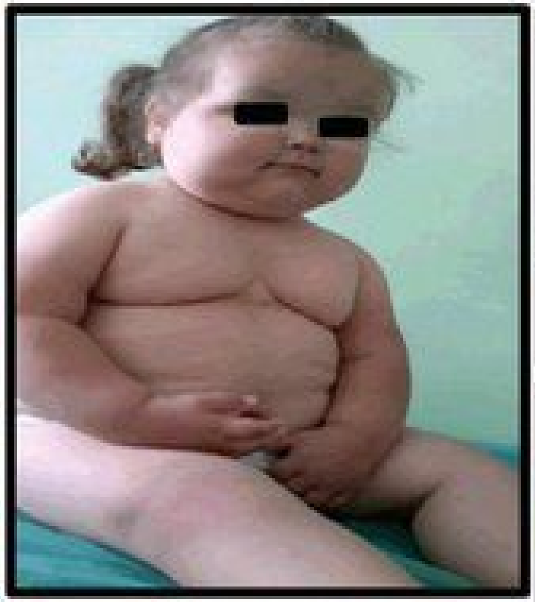
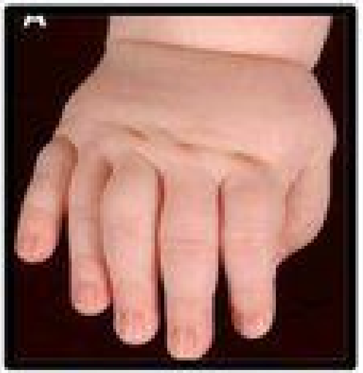
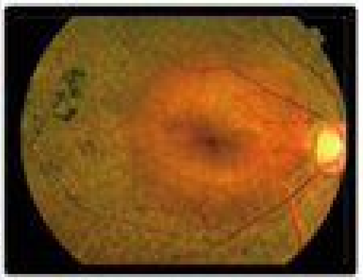
❖ **Common cardiac defect ?**
- ✓ **VSD, ASD, PDA & TOF**

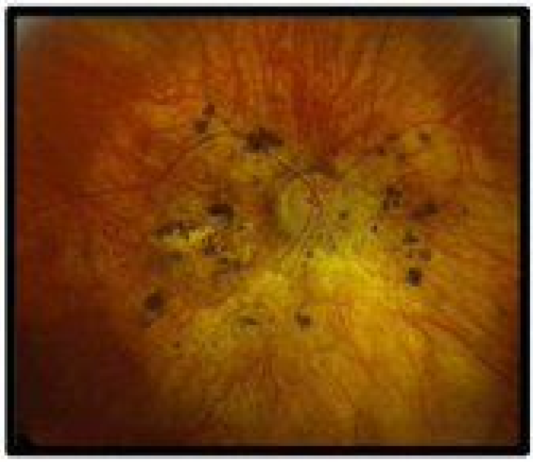
Pediatric On Squares

17) Bardet–Biedl syndrome (Laurence-Moon-Biedl syndrome)







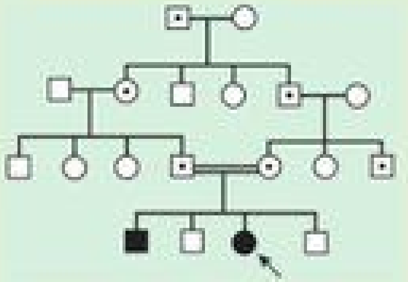


❖ Clinical features

- ✓ Obesity
- ✓ Postaxial polydactyly
- ✓ Hypogonadism
- ✓ Retinitis pigmentosa
- ✓ Rod-cone dystrophy
- ✓ Mental retardation
- ✓ Polyuria and polydipsia
- ✓ Renal anomalies

❖ Mode of inheritance?

- ✓ Autosomal recessive



❖ Most common gastrointestinal association?

- ✓ Hirschsprung disease

❖ What is the cause of polyuria and polydipsia?

- ✓ Nephrogenic diabetes insipidus

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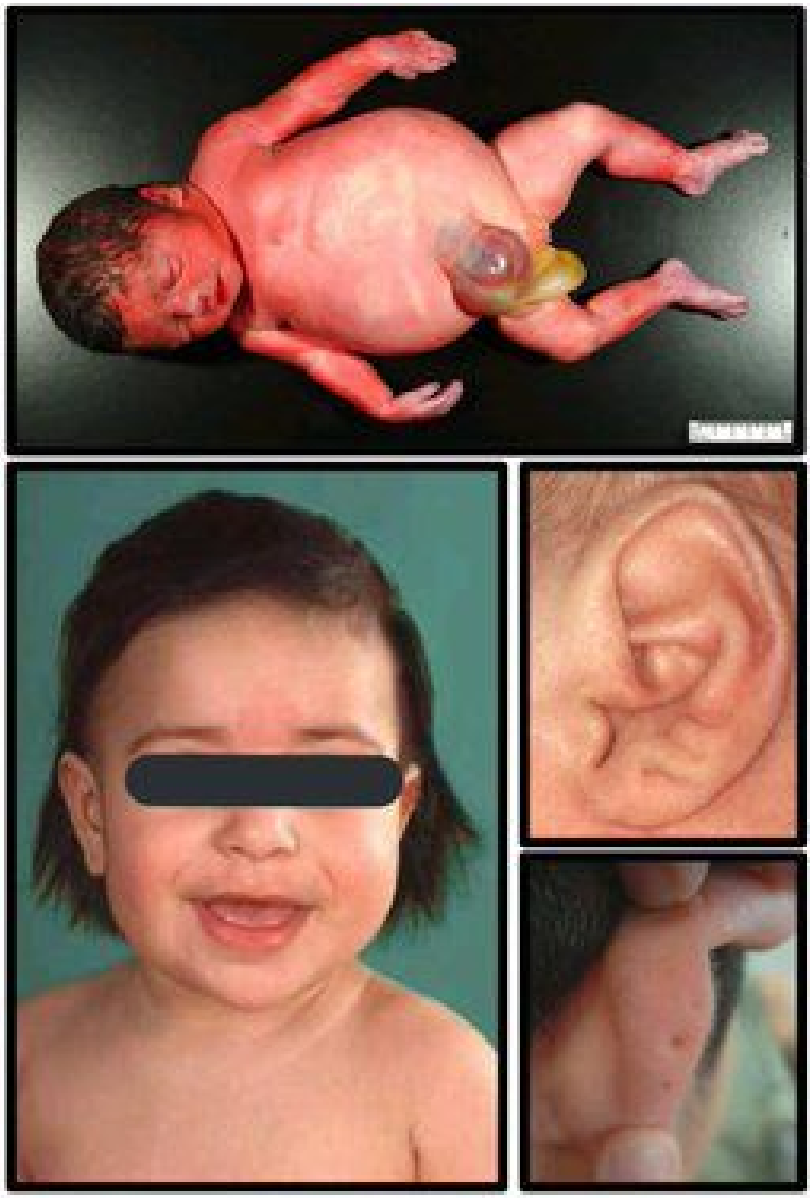


16) Beckwith-Wiedemann syndrome

❖ Clinical features

- ✓ Large for gestational age
- ✓ Macroglossia
- ✓ Omphalocele
- ✓ **Ear lobe creases**
- ✓ **Posterior auricular pits**
- ✓ Hemihypertrophy
- ✓ Cryptorchidism
- ✓ Umbilical hernia
- ✓ Normal intelligence

❖ Laboratory finding ?

- ✓ Hypoglycemia
- ✓ Hyperinsulinism
  - ➢ Due pancreatic islet hyperplasia

❖ Mode of inheritance?

- ✓ Sporadic
- ✓ Autosomal dominant
- ✓ 15q11 deletion

❖ Increases risk of which Malignancies ?

- ✓ Wilms tumor
- ✓ Hepatoblastoma

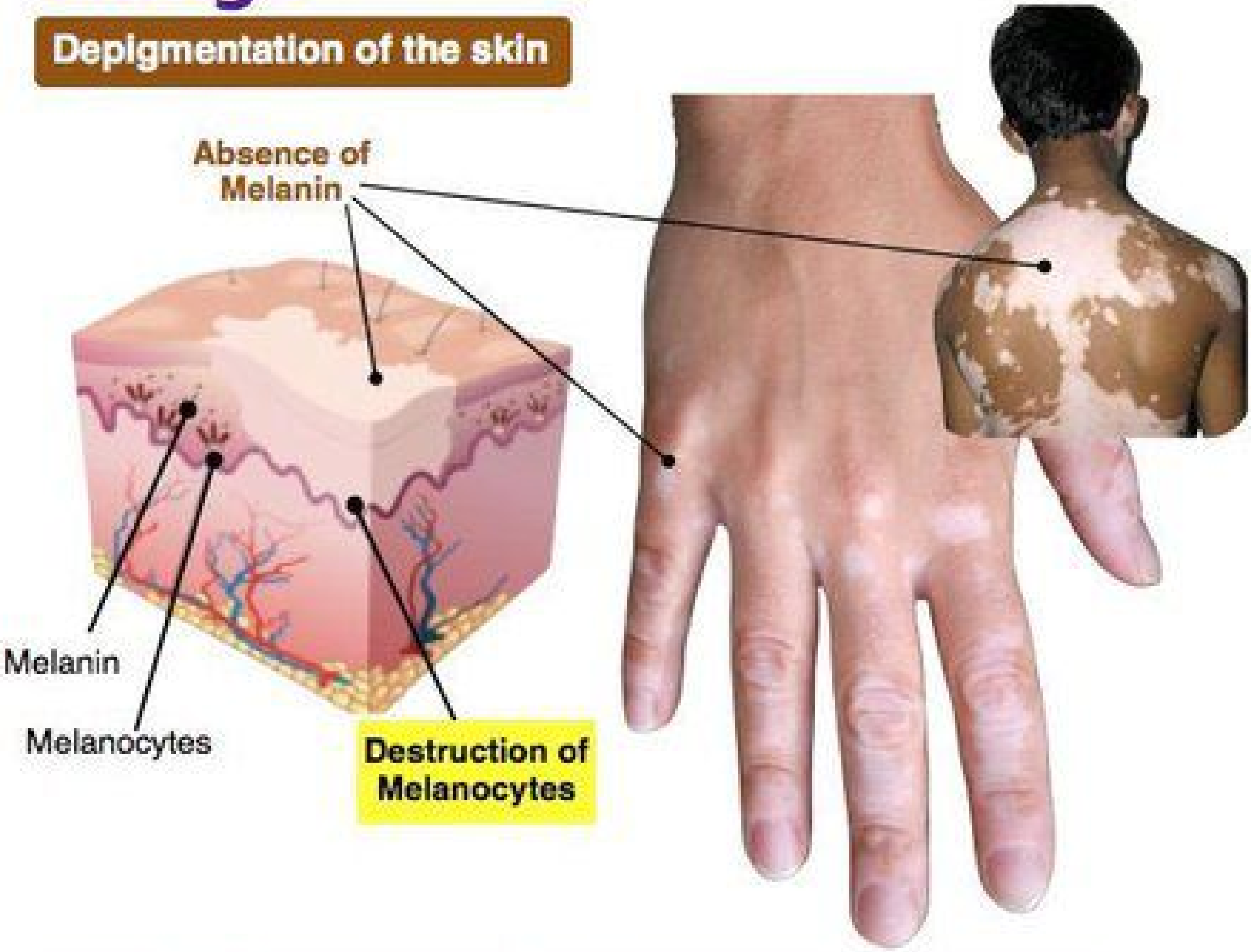
❖ Clinic follow up ?

- ✓ **Abdominal US**
  - Q3 months until 4 Y.O
- ✓ **Alpha fetoprotein**
  - Q3 months until 4 Y.O
- ✓ **Renal US**
  - Q3 months from 4-7 Y.O

@OnSquares

Vitiligo

Depigmentation of the skin


Absence of Melanin
Melanin
Melanocytes
Destruction of Melanocytes

Frequently associated with Autoimmune thyroid disease

- Alopecia aerate
- Psoriasis
- Type 1 diabetes
- Rheumatoid arthritis
- Inflammatory bowl disease
- Pernicious anemia
- Myasthenia gravis
- Lupus
- Sjögren syndrome

Management

- Psychosocial support

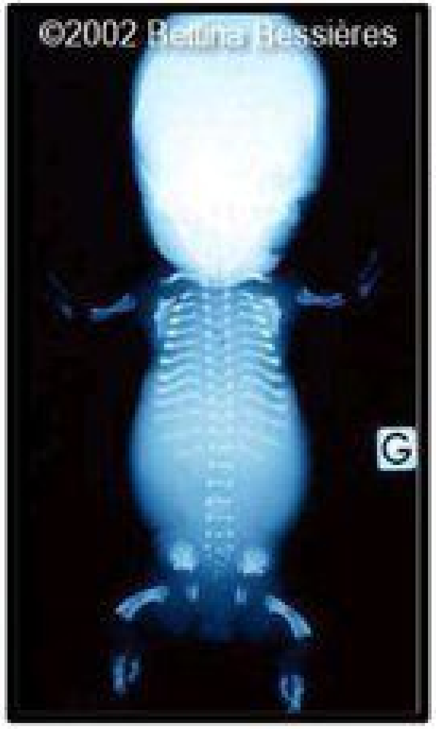
Stabilization

- Oral corticosteroids, NB-UVB phototherapy
- Minocycline, Methotrexate, Vitamin supplementation

Regimentation

- Topic corticosteroids, Calcineurin inhibitors, Vitamin D analogues
- Phototherapy

21) Thanatophoric Dysplasia


©2002 Bettina Bessières

Clinical features

- Rhizomelic Shorting
- Small chest
- Absent sciatic notch.
- Platyspondyly (flattened vertebral bodies).
- French-telephone femurs.
- H-shaped vertebrae.
- Cloverleaf skull (severe craniosynostosis).

Pediatric On Squares
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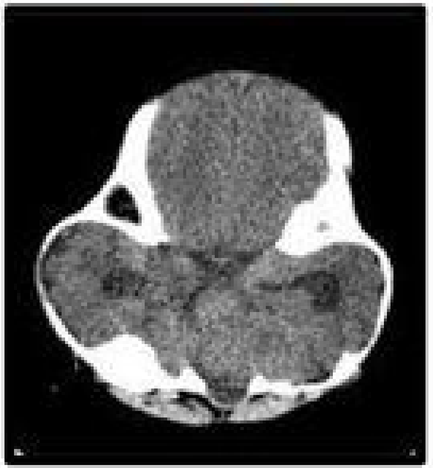
❖ **Mode of inheritance?**

- ✓ Autosomal Dominant
- ✓ Defect in FGFR-3

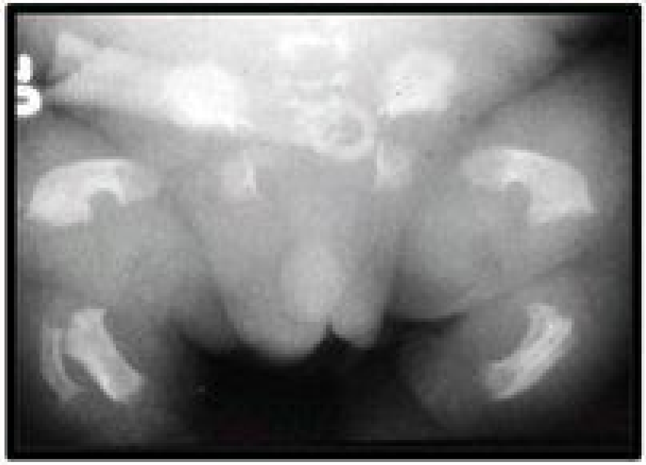
❖ **Most common cause of death?**

- ✓ Craniocervical junction compression
- ✓ Pulmonary hypoplasia

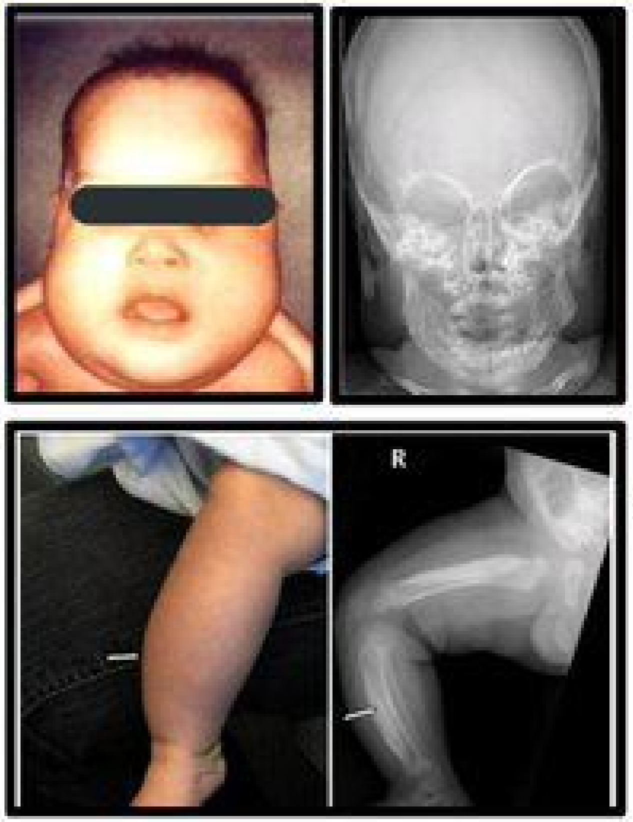


❖ **Types**

- Type I
  - Without cloverleaf skull
  - Telephone receiver femur
- Type II
  - With cloverleaf skull
  - Straight femur



22) Infantile cortical hyperostosis (Caffey Disease)



The bone changes typically begin before six months of age and resolve by two years.

Clinical features

- Extreme irritability.
- Soft tissue swelling.
- Fever.
- Anorexia.
- Cortical thickening of bones.
- Pseudoparalysis

Differential diagnosis

- Osteomyelitis
- Hypervitaminosis A.
- Child abuse.
- Leukemia

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❖ Most common affected bone?

✓ **Mandible**

❖ Mode of inheritance?

✓ Autosomal dominant
✓ COL1A1 gene

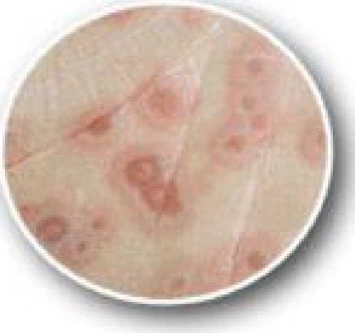
❖ Laboratory finding ?

✓ Leukocytosis
✓ Thrombocytosis
✓ High ESR
✓ High Alkaline phosphatase

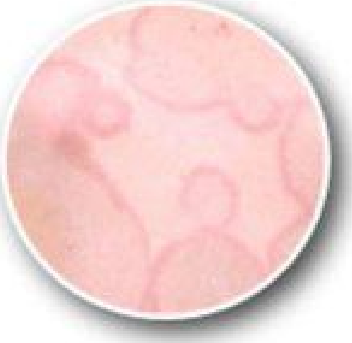
❖ Prognosis

✓ Self-limited condition
✓ Deformities of the involved bones.

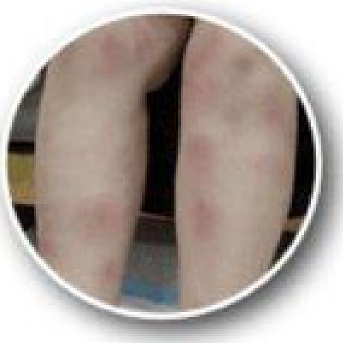
"Erythema" Rashes



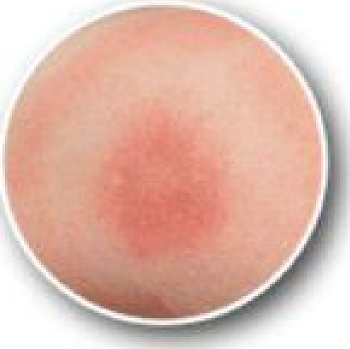
Erythema multiforme
Target-like lesions
Infectious, medication, autoimmune



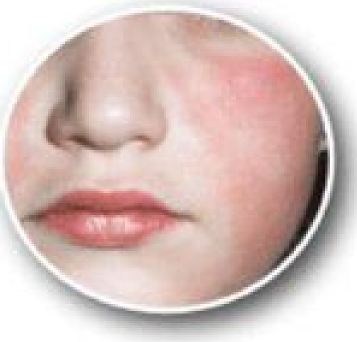
Erythema marginatum
Macule with central clearing
Spares the face
Rheumatic fever



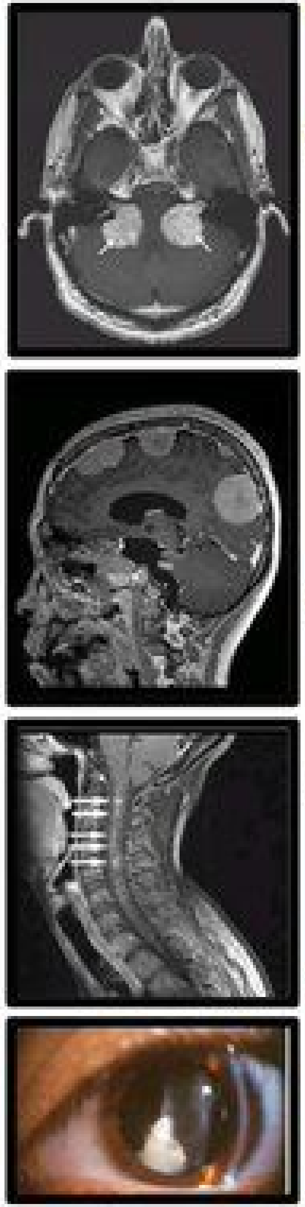
Erythema nodosum
Inflammatory nodules
Infectious, autoimmune, medication, pregnancy



Erythema migrans
Bull's eye appearance
Lyme disease



Erythema infectiosum
Slapped cheek appearance
Circumoral pallor
Parvovirus B19 infection



38) Neurofibromatosis type 2 (MISME syndrome)

❖ **Diagnostic criteria** (1 of the following sets)

- ✓ Bilateral vestibular schwannomas (acoustic neuromas)
- ✓ Unilateral vestibular schwannoma AND first-degree relative with NF2.
- ✓ Unilateral vestibular schwannoma Or first-degree relative with NF2 AND any 2 of the following:
  - Meningioma
  - Nonvestibular schwannoma
  - Ependymoma
  - Cataract

Other clinical features

- ✓ Hearing loss
- ✓ Tinnitus

❖ **What is 1st manifestation typically appears ?**

✓ Cataract

❖ **What is most common type of tumor in NF2?**

✓ Schwannomas

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❖ **What is most common affected cranial nerve with schwannomas?**

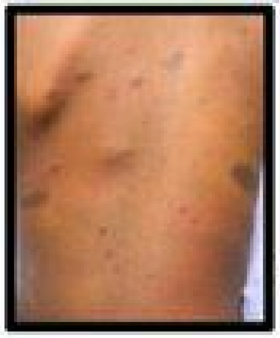
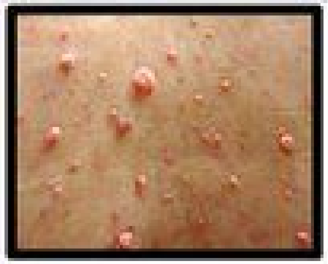
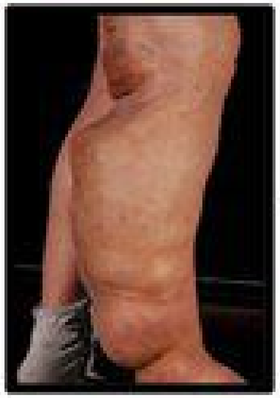
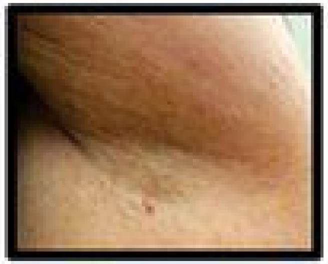
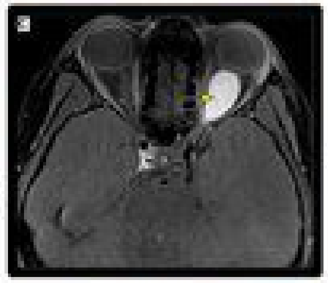
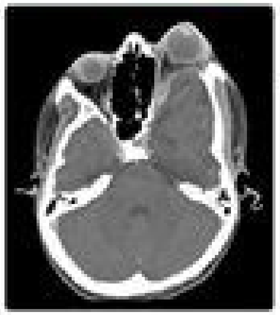
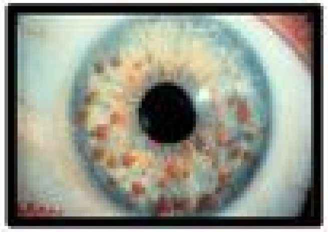
✓ CN VIII (vestibulocochlear nerve)

❖ **Mode of inheritance?**

- ✓ Autosomal dominant
- ✓ NF2 gene on chromosome 22

- Café-au-lait macules can be seen but are much less frequent in NF2.
- NF2 is not associated with the cognitive impairment that is often seen with NF1.

37) Neurofibromatosis type 1 (von Recklinghausen disease)

❖ **Diagnostic criteria** (≥ 2 of the following)

- ✓ ≥ 6 café-au-lait macules
  - > 5 mm in in prepubertal
  - > 15 mm in in postpubertal
- ✓ ≥ 2 neurofibromas or 1 plexiform neurofibroma
- ✓ Axillary or inguinal freckling (Crowe sign)
- ✓ Optic glioma
- ✓ ≥ 2 iris hamartoma (Lisch nodules)
- ✓ Distinctive bony lesion:
  - Sphenoid dysplasia, or
  - Tibial pseudoarthrosis, or
  - Cortical thickening of the long bone
- ✓ A first-degree relative with NF1

❖ **What is 1st manifestation typically appears ?**

- ✓ Café-au-lait macules

❖ **What is most common type of benign tumor in NF1 ?**

- ✓ Neurofibromas

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❖ **Mode of inheritance?**

- ✓ AD (50%)
- ✓ De novo (50%)
- ✓ NF1 gene on chromosome 17

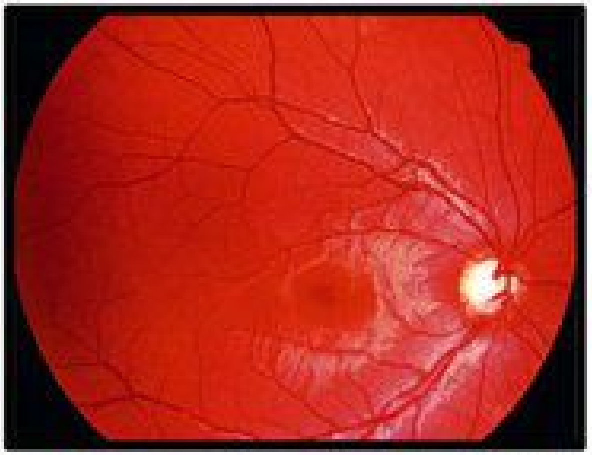
❖ **Increases risk of :**

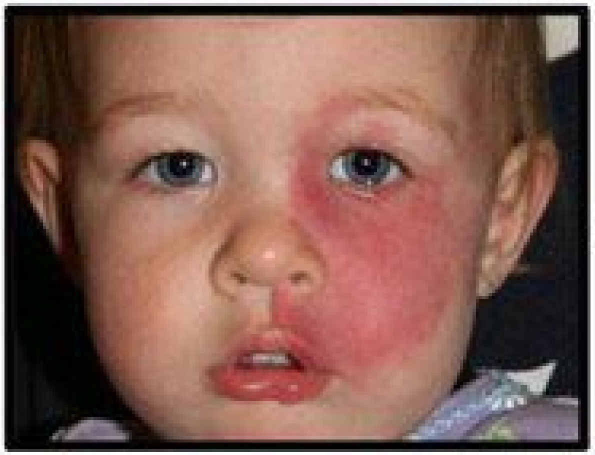
- ✓ **Malignancies**
- ✓ Primary HTN
- ✓ Learning disabilities
- ✓ Seizures

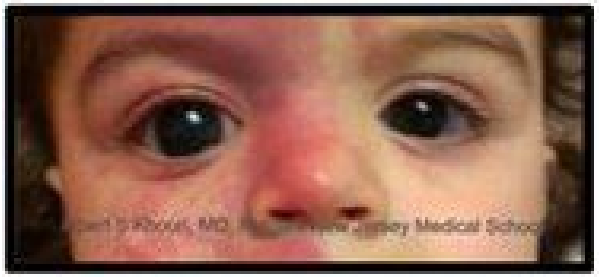
❖ **Follow up :**

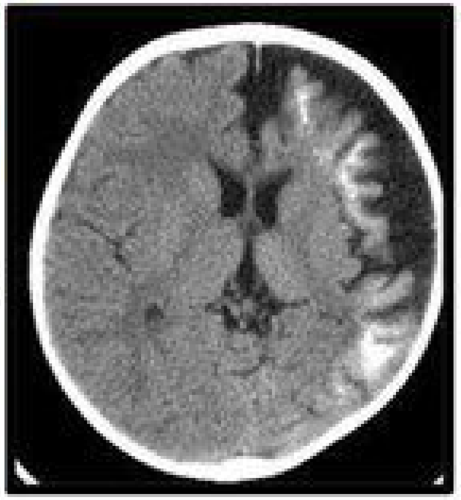
- ✓ Annual vision exam
- ✓ BP monitoring
- ✓ Annual full physical examination
- ✓ Tumor surveillance

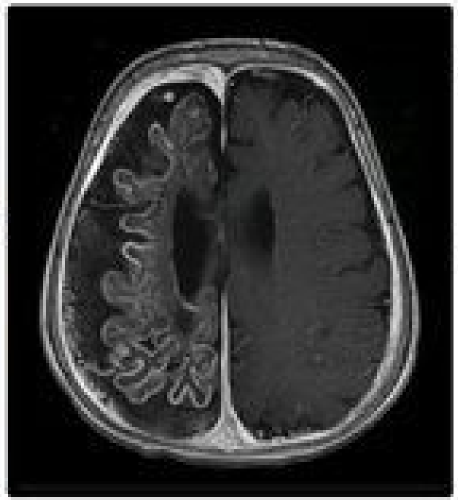
40) Sturge Weber syndrome











❖ Clinical features

- ✓ Port wine stain (1st & 2nd division of trigeminal nerve)
- ✓ Ipsilateral leptomeningeal angioma
- ✓ Glaucoma
- ✓ Diffuse choroidal hemangioma
- ✓ Seizures (on contralateral side)
- ✓ Focal neurologic deficits
- ✓ Buphthalmos
- ✓ Intellectual disability.

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❖ Mode of inheritance?

- ✓ Not inherited, due somatic mutation

❖ What is the best neuroimaging diagnostic study?

- ✓ Brain MRI with gadolinium contrast
- ✓ Tram track calcification

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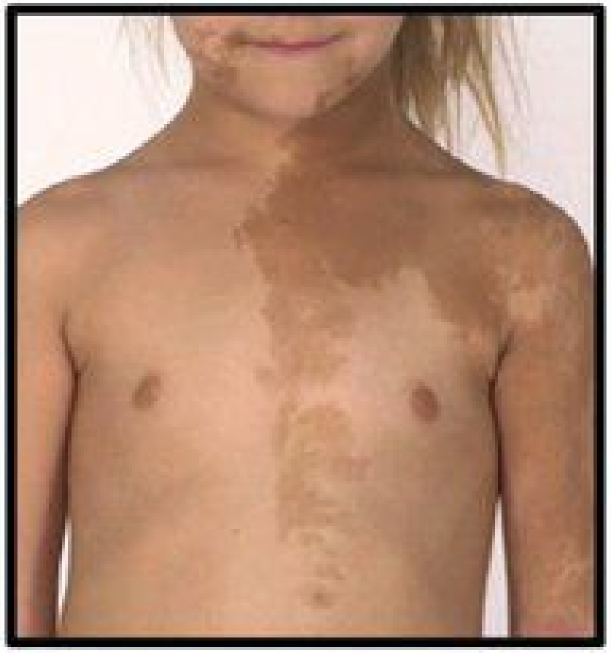
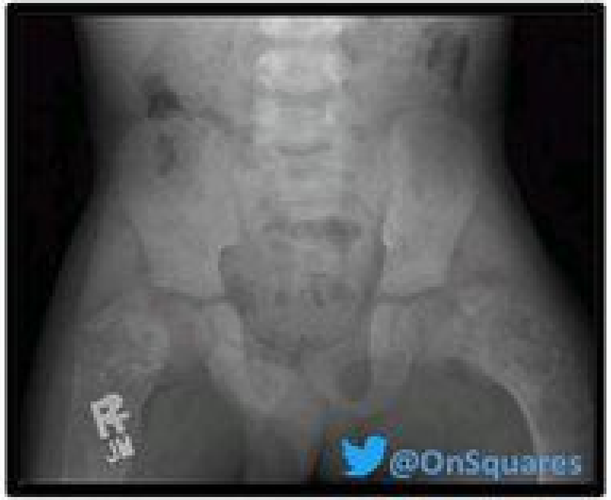




41) McCune-Albright syndrome (MAS)

❖ Clinical features

Classic triad

- ✓ Precocious puberty
- ✓ Café-au-lait macules
- ✓ Polyostotic fibrous dysplasia

❖ What is the classic presenting sign of Precocious puberty in MAS?

- ✓ Vaginal bleeding

❖ What is the other common endocrine association in MAS?

- ✓ Hyperthyroidism

❖ Mode of inheritance?

- ✓ Sporadic
- ✓ Mutation in the GNAS1 gene
- ✓ More common in girls

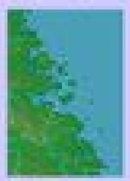
❖ What is the most characteristic laboratory finding?

- ✓ High growth hormone
- ✓ High prolactin
- ✓ High luteinizing hormone (LH)
- ✓ High follicle-stimulating hormone (FSH)
- ✓ Hypophosphatemia & hyperphosphaturia

❖ How to differentiated café-au-lait macules from those of neurofibromatosis (NF)

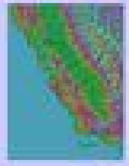
In MAS

- ✓ Coast of Maine borders
- ✓ Irregular borders
- ✓ Never cross midline



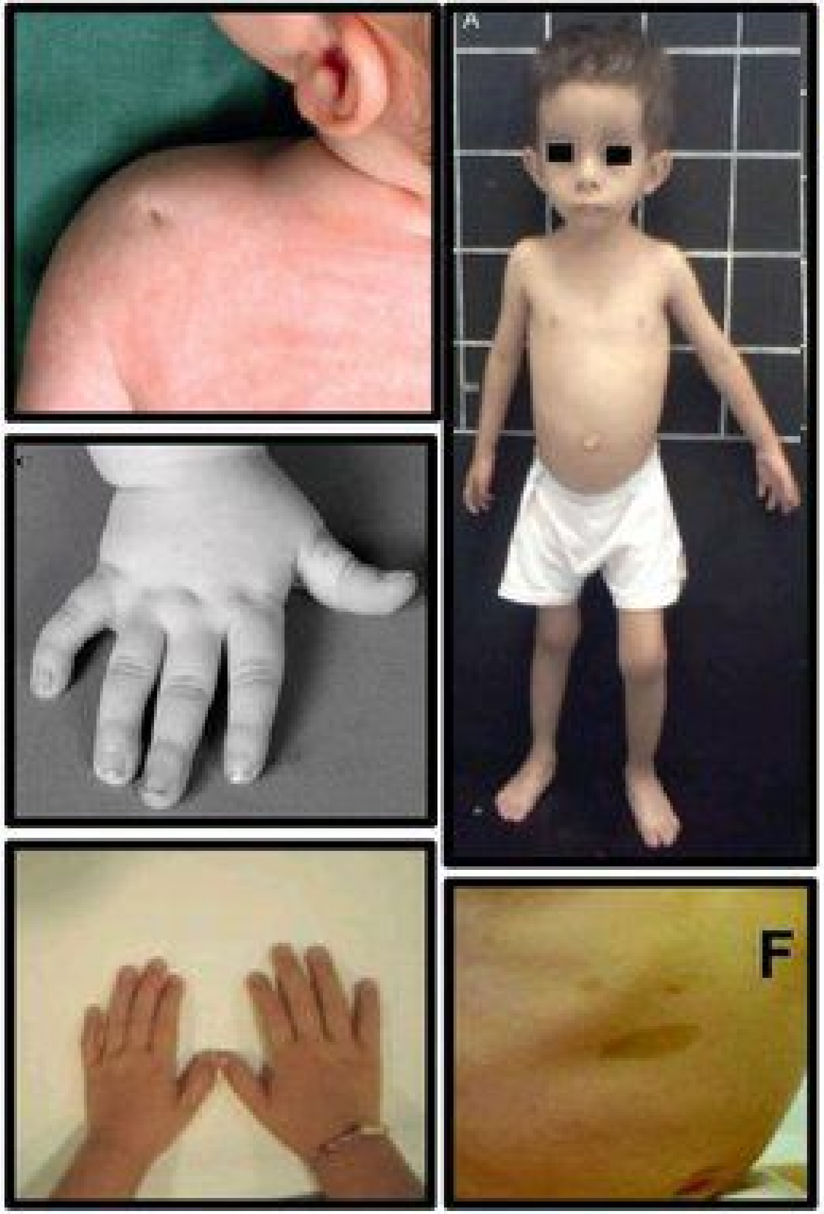
In NF

- ✓ Coast of California
- ✓ Smooth borders
- ✓ Cross midline



❖ Treatment

- ✓ GnRH agonist
- ✓ Oral phosphate and calcitriol



42) Russel Silver syndrome

❖ Clinical features

- ✓ Short stature
- ✓ Small for gestational age
- ✓ Hemihypertrophy
- ✓ Pseudohydrocephlus
- ✓ Triangular face
- ✓ Inverted V shaped mouth
- ✓ Crap shape mouth
- ✓ Café au lait macules
- ✓ 5th finger Clinodactyly
- ✓ Syndactyly
- ✓ Excessive sweating
- ✓ Male genital abnormalities
- ✓ High-pitched voice
- ✓ Shoulder dimples
- ✓ Failure to thrive
- ✓ Speech delay

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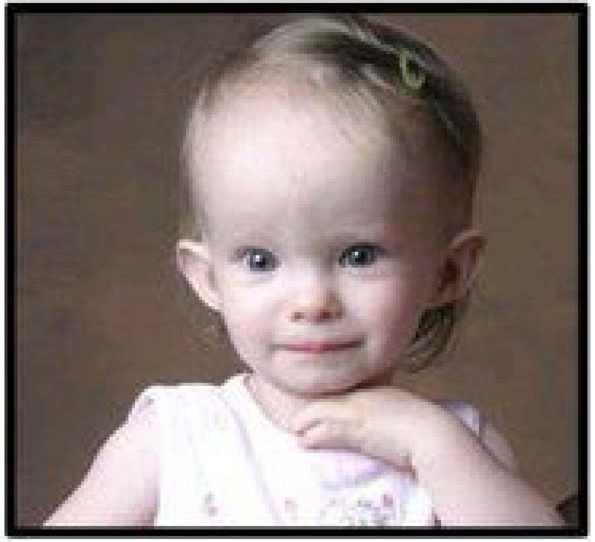
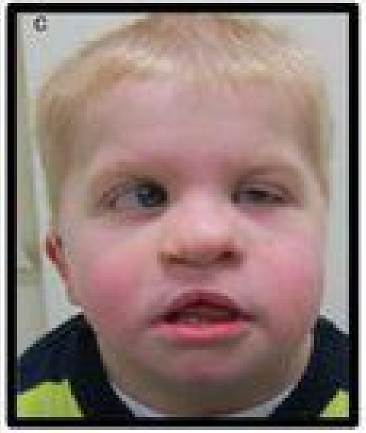
❖ Mode of inheritance?

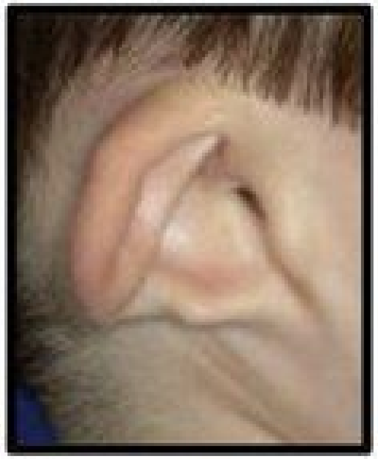
- ✓ Hypomethylation of IGF-2, or
- ✓ Maternal UPD of chromosome 7

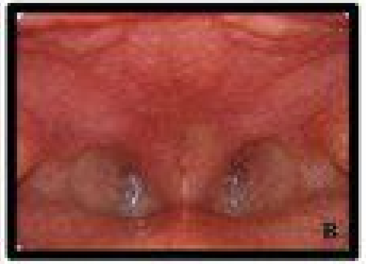
❖ Laboratory finding ?

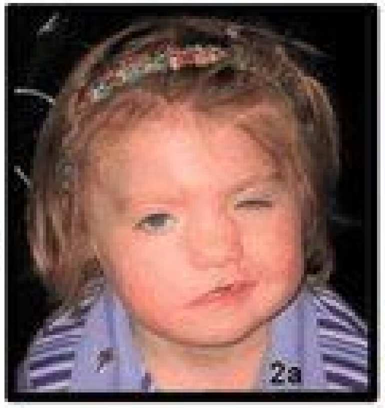
- ✓ Hypoglycemia

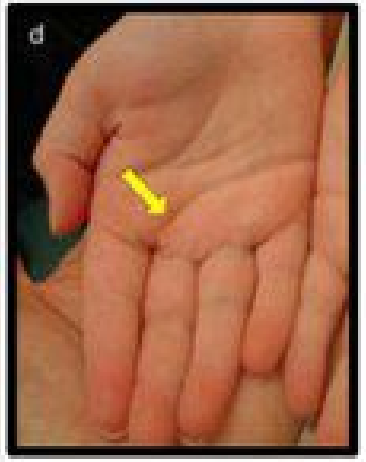


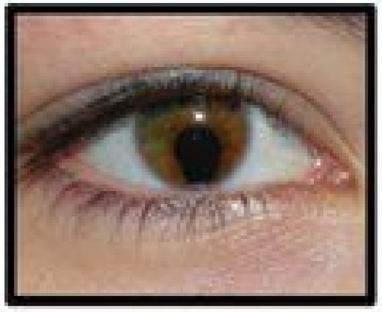












43) CHARGE Syndrome

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❖ Diagnostic criteria

Major criteria

- ✓ Ocular colobomas
- ✓ Choanal atresia
- ✓ Cranial nerve dysfunction (Anosmia, facial palsy, auditory nerve hypoplasia)
- ✓ Ear anomalies

Minor criteria

- ✓ Genital hypoplasia
- ✓ Developmental delay
- ✓ Cardiovascular anomalies
- ✓ Cleft lip and/or palate
- ✓ Tracheoesophageal fistula or esophageal atresia
- ✓ Facial dysmorphology (Square face, prominent forehead, flat midface)
- ✓ Growth failure
- ✓ 'J'-shaped hockey stick palmar crease

Definite CHARGE syndrome:
- ✓ 4 major Or
- ✓ 3 major and 3 minor

Probable CHARGE syndrome:
- ✓ 1 or 2 major and several minor.

❖ Mode of inheritance?

- ✓ Autosomal dominant
- ✓ CHD7 gene

❖ What is the most common cardiac defect?
- ✓ Tetralogy of fallot
- ✓ Conotruncal defect
- ✓ Arch anomalies

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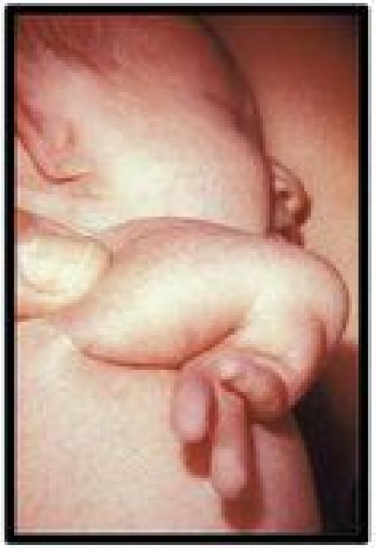

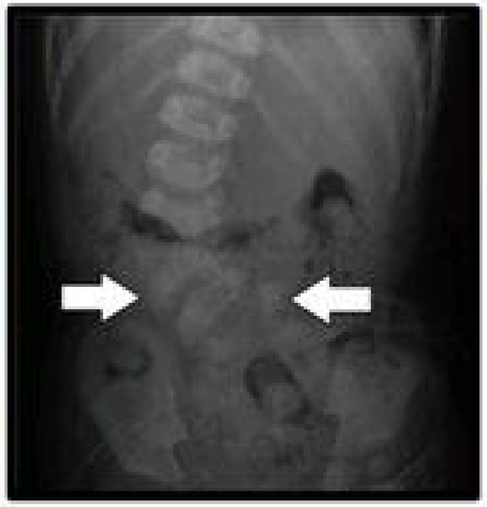

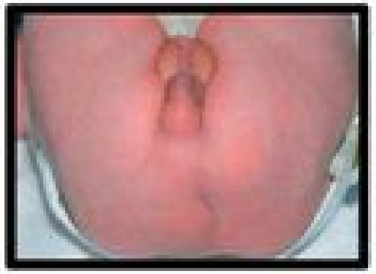

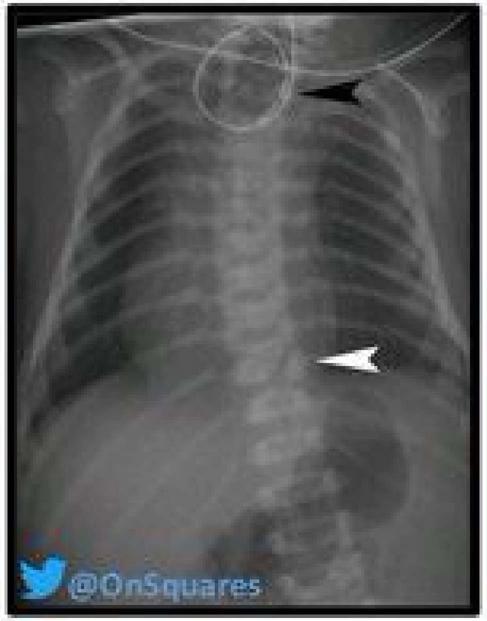

44) VACTERL association

❖ Clinical features

- ✓ Vertebral defect
- ✓ Anal atresia
- ✓ Congenital heart defect
- ✓ Tracheoesophageal fistula
- ✓ Esophageal Atresia
- ✓ Renal anomalies
- ✓ Limb (radial) hypoplasia

±

- ✓ Single umbilical artery

❖ How to confirm the diagnosis?

- ✓ Clinically
- ✓ ≥ 3 features

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❖ Mode of inheritance?

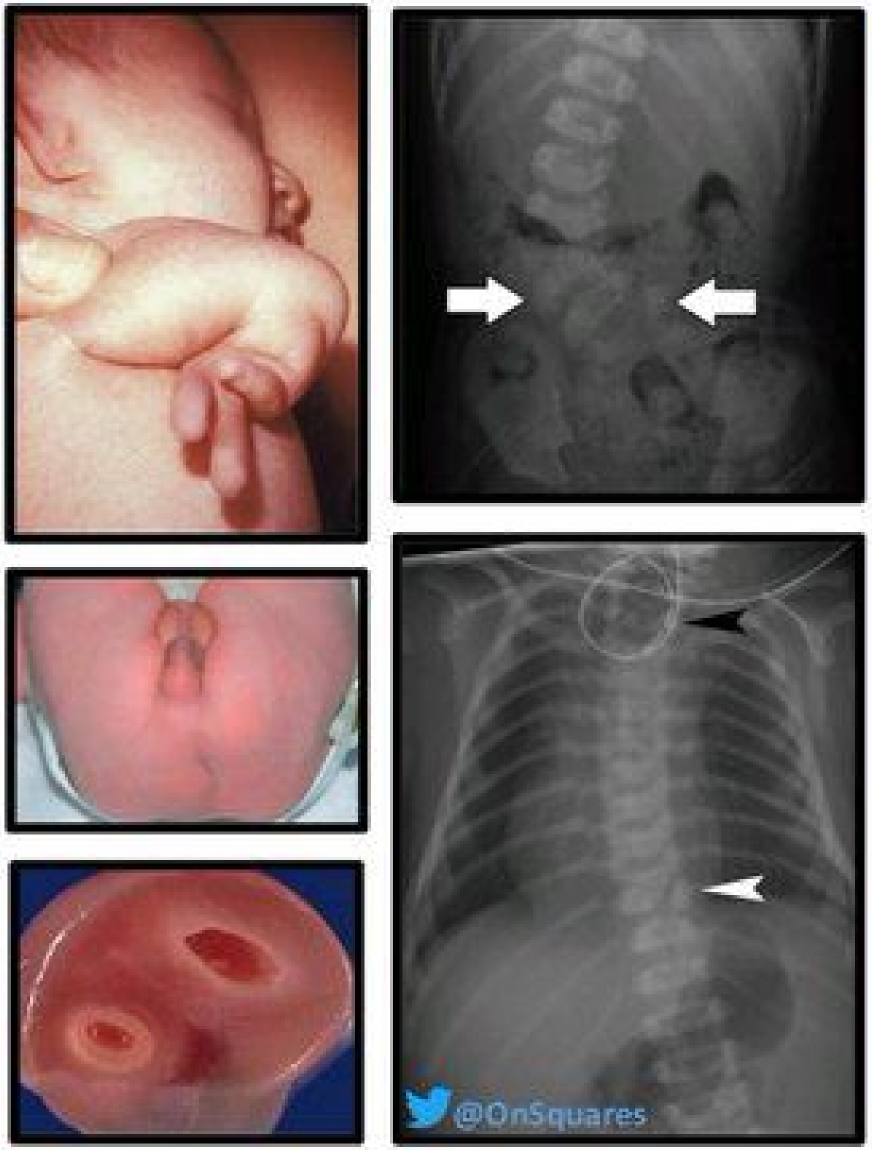
- ✓ Sporadic

❖ What is the most common cardiac defect?

- ✓ **VSD**
- ✓ TOF
- ✓ ASD
- ✓ PDA

❖ What is the level of intelligence ?

- ✓ Normal
- Note CHARGE have intellectual disability



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Pediatric On Squares

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- ✓ **VSD**
- ✓ TOF
- ✓ ASD
- ✓ PDA

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- ✓ Normal
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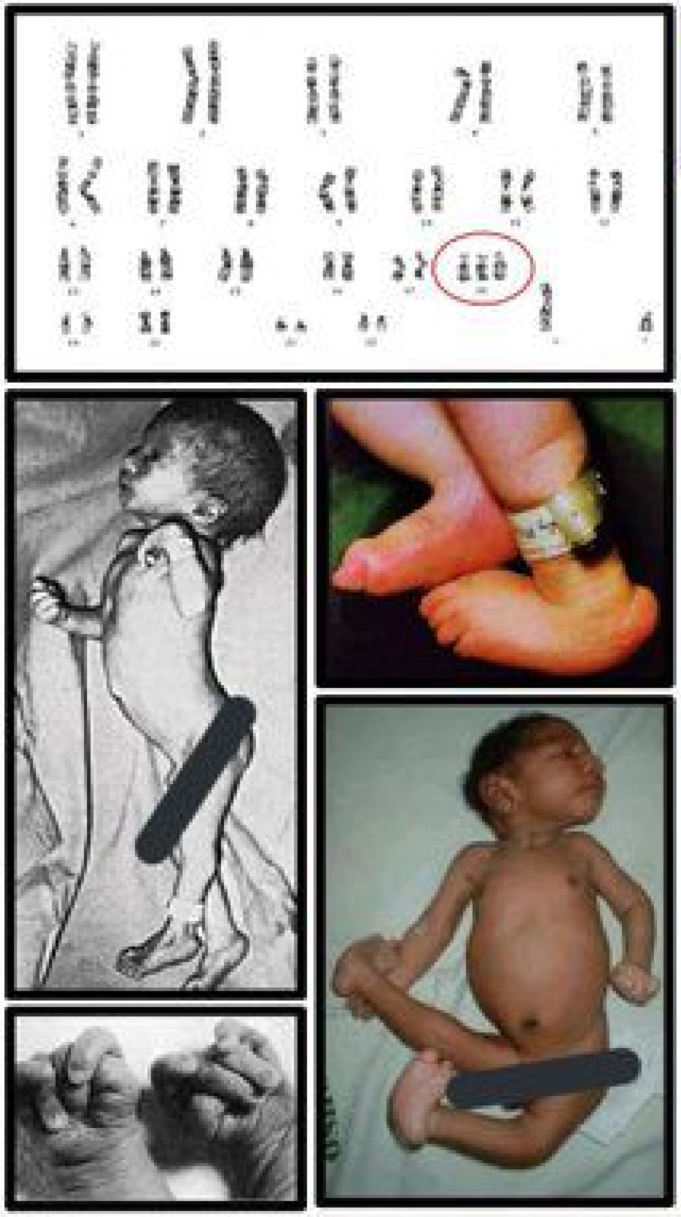
2) Trisomy 18 (Edwards syndrome)



❖ Clinical features

- ✓ **Rocker bottom feet**
- ✓ **Overlapping fingers**
- ✓ **Clenched fist**
- ✓ Short sternum
- ✓ Hypoplastic nails
- ✓ Hypoplastic nasal alae
- ✓ IUGR
- ✓ Intellectual disability
- ✓ Microcephaly
- ✓ Hypertonia
- ✓ Prominent occiput
- ✓ Micrognathia
- ✓ Limited hip abduction
- ✓ Cleft lip / palate

2nd most common autosomal trisomy

❖ Most common cardiac defect ?

- ✓ **Ventricular septal defect (VSD)**
- ✓ Atrial septal defect (ASD)
- ✓ PDA

❖ Most common cause of death?

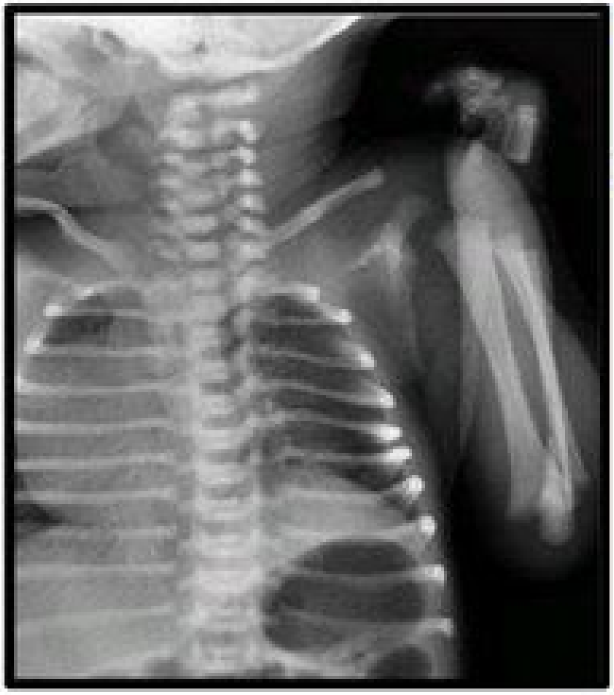
- ✓ Central apnea

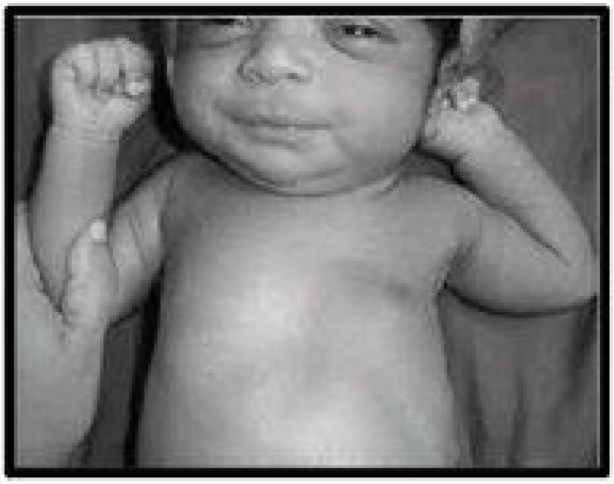
❖ Prenatal screen lab finding?

- ✓ Low α feto protein
- ✓ Low estriol
- ✓ Low hCG

❖ Prognosis

- ✓ 50% die in the 1st week of life
- ✓ 90% die by 1 year of age





45) Poland Syndrome

- **Clinical features**
  - ✓ Unilateral absence of the pectoralis muscle.
  - ✓ Aplasia of ipsilateral
    - Ribs
    - Costal cartilages
    - Nipples
  - ✓ Abnormalities of ipsilateral proximal & distal upper extremity
  - ✓ Dextrocardia
  - ✓ Diaphragmatic hernia

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- **Which maternal disease increase the risk of Poland syndrome?**
  - ✓ Maternal diabetes.

- **Mode of inheritance?**
  - ✓ Not inherited, unknown cause

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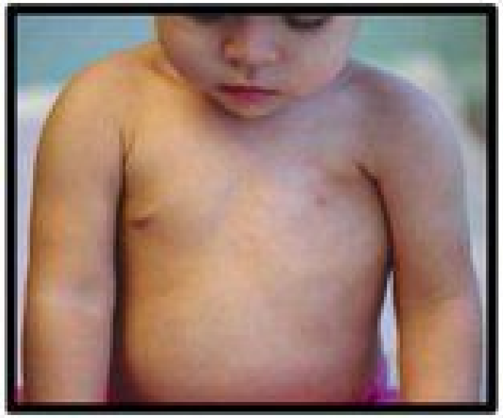
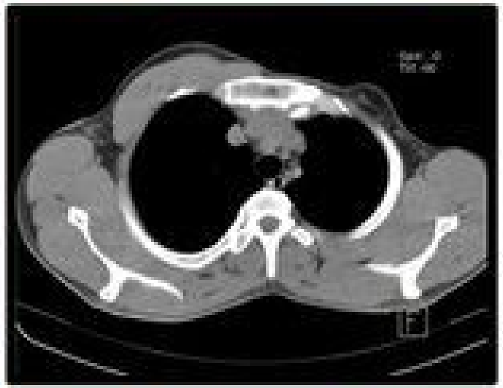
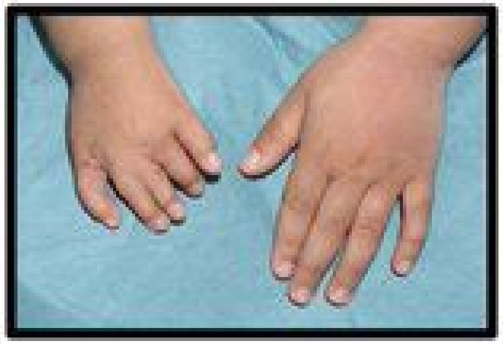
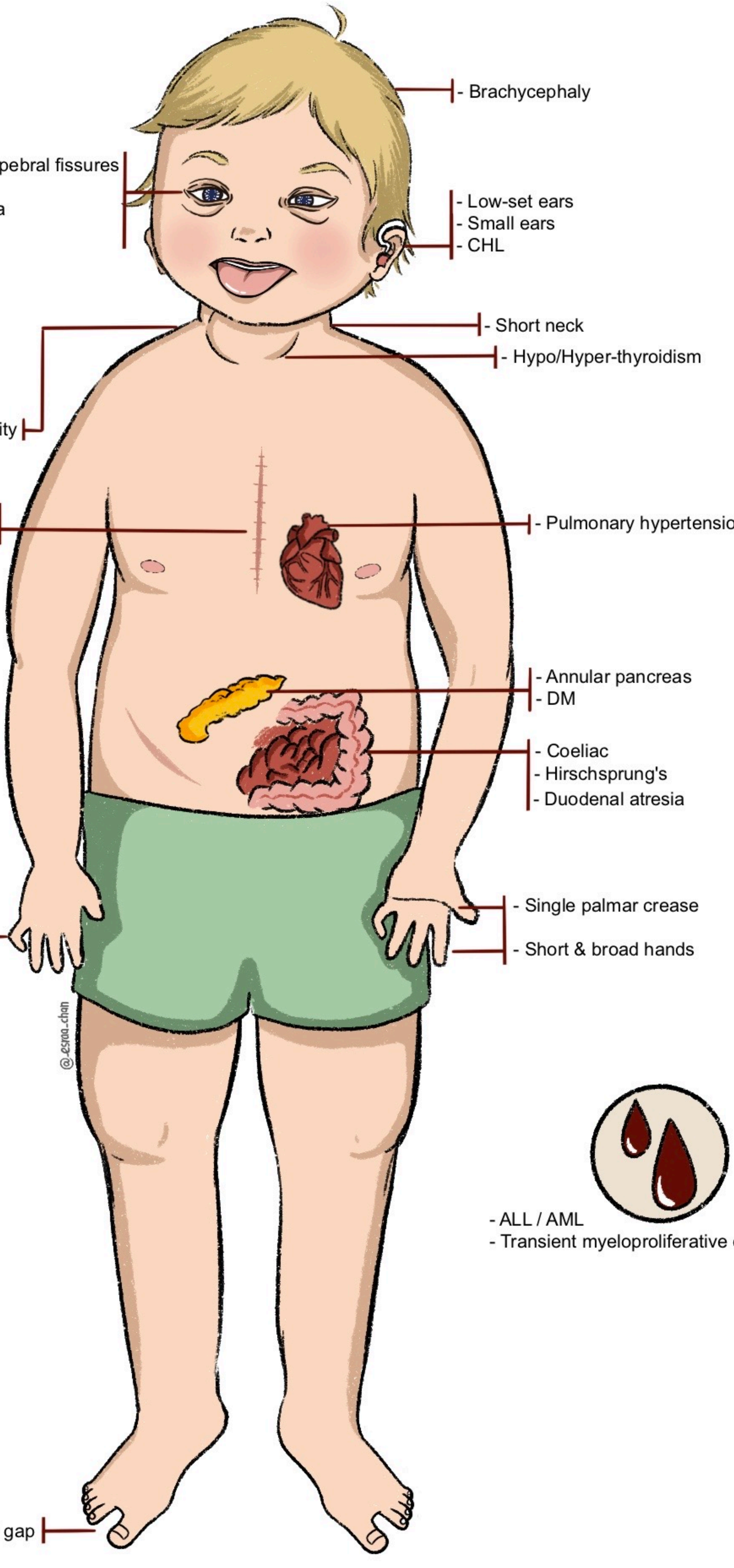






Down Syndrome



- Brachycephaly

- Upward slanting palpebral fissures
- Brushfield spots
- Cataract / Glaucoma
- Strabismus

- Low-set ears
- Small ears
- CHL

- Short neck
- Hypo/Hyper-thyroidism

- Atlanto-axial laxity

- AVSD
- VSD

- Pulmonary hypertension

- Annular pancreas
- DM

- Coeliac
- Hirschsprung's
- Duodenal atresia

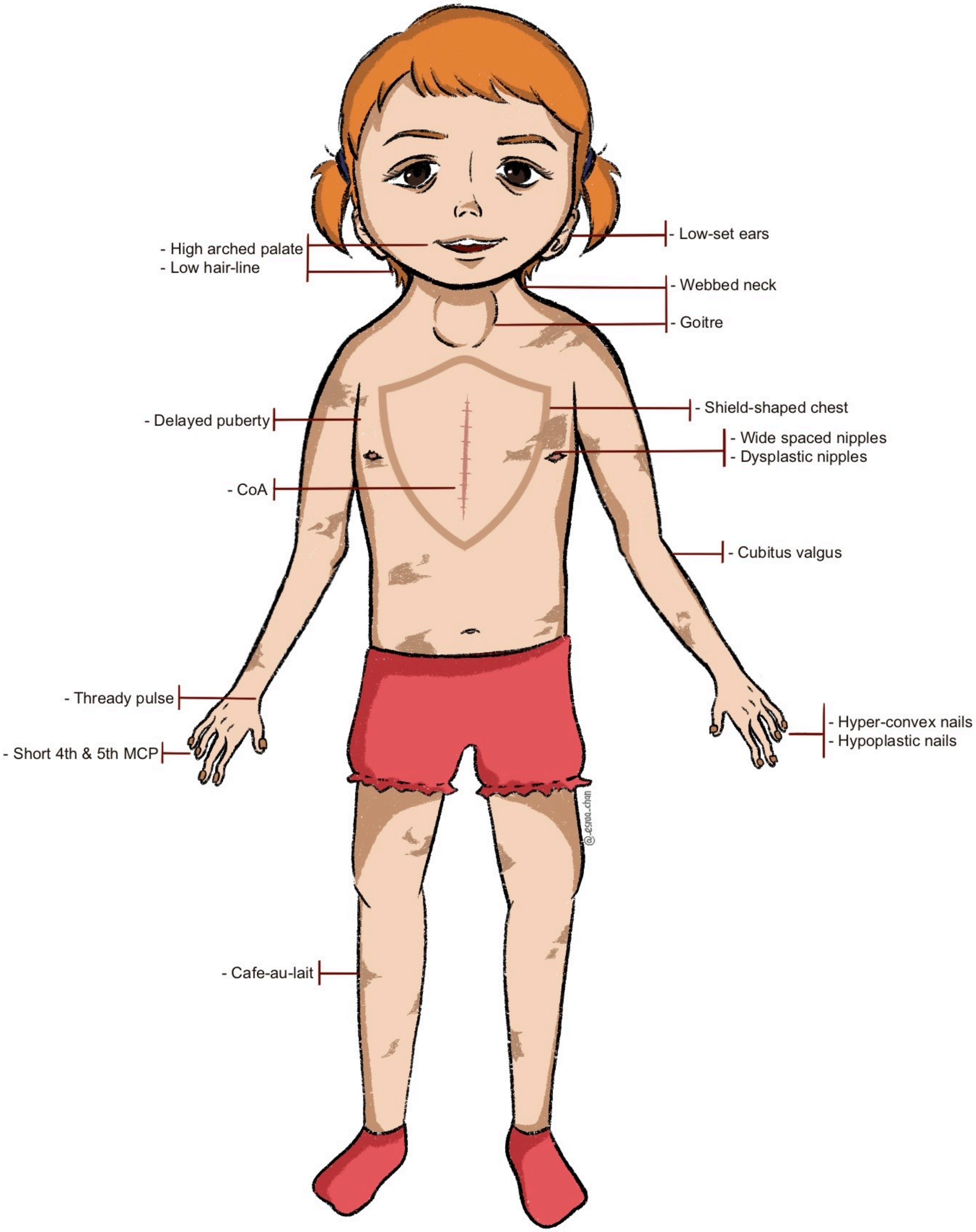
- Single palmar crease
- Short & broad hands

- Clinodactyly

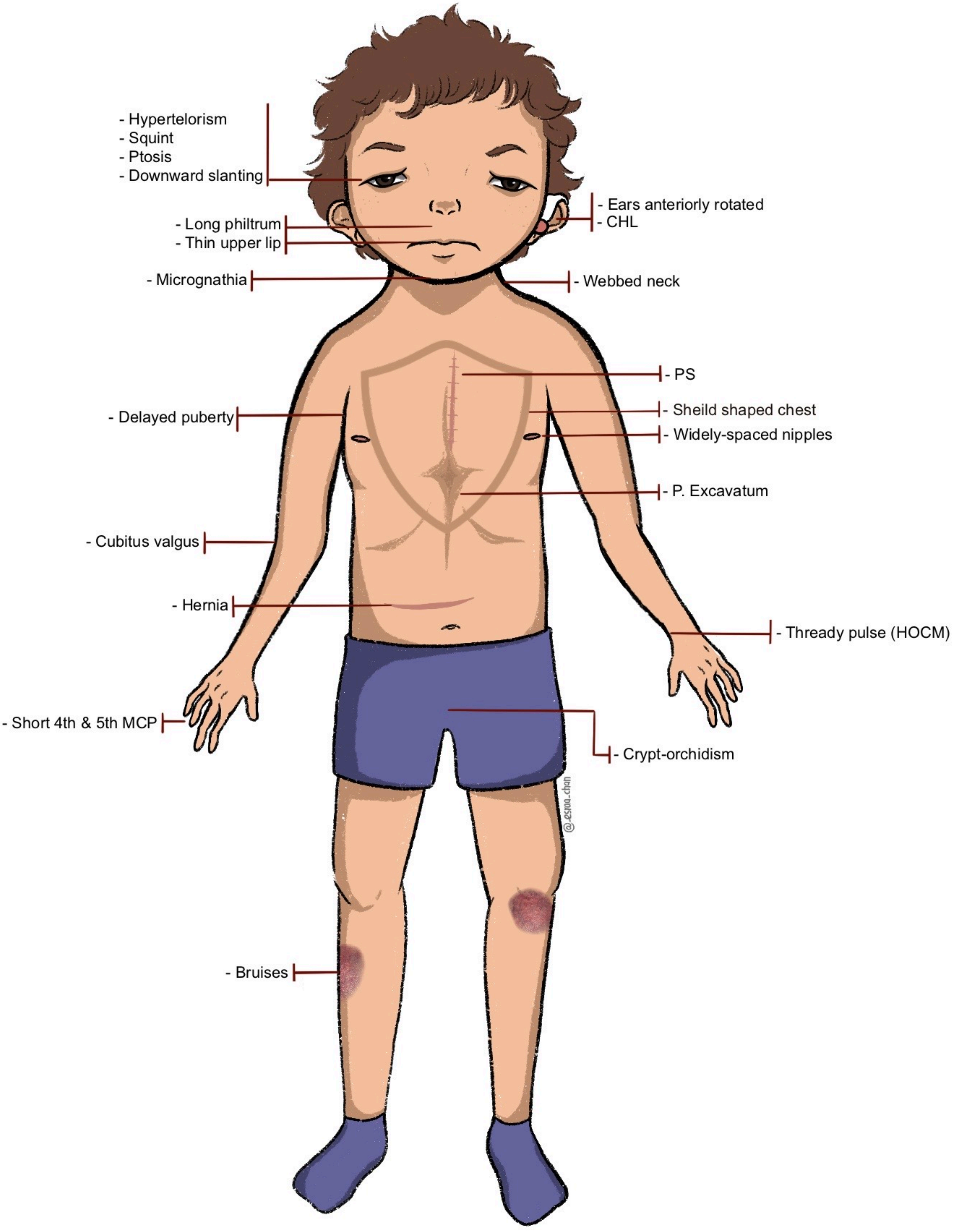
- ALL / AML
- Transient myeloproliferative disorders

- Sandal gap

Turner Syndrome


- Low-set ears
- High arched palate
- Low hair-line
- Webbed neck
- Goitre
- Shield-shaped chest
- Delayed puberty
- Wide spaced nipples
- Dysplastic nipples
- CoA
- Cubitus valgus
- Thready pulse
- Hyper-convex nails
- Hypoplastic nails
- Short 4th & 5th MCP
@_esraa_chan
- Cafe-au-lait

Noonan Syndrome


- Hypertelorism
- Squint
- Ptosis
- Downward slanting
- Ears anteriorly rotated
- CHL
- Long philtrum
- Thin upper lip
- Micrognathia
- Webbed neck
- PS
- Sheild shaped chest
- Delayed puberty
- Widely-spaced nipples
- P. Excavatum
- Cubitus valgus
- Hernia
- Thready pulse (HOCM)
- Short 4th & 5th MCP
- Crypt-orchidism
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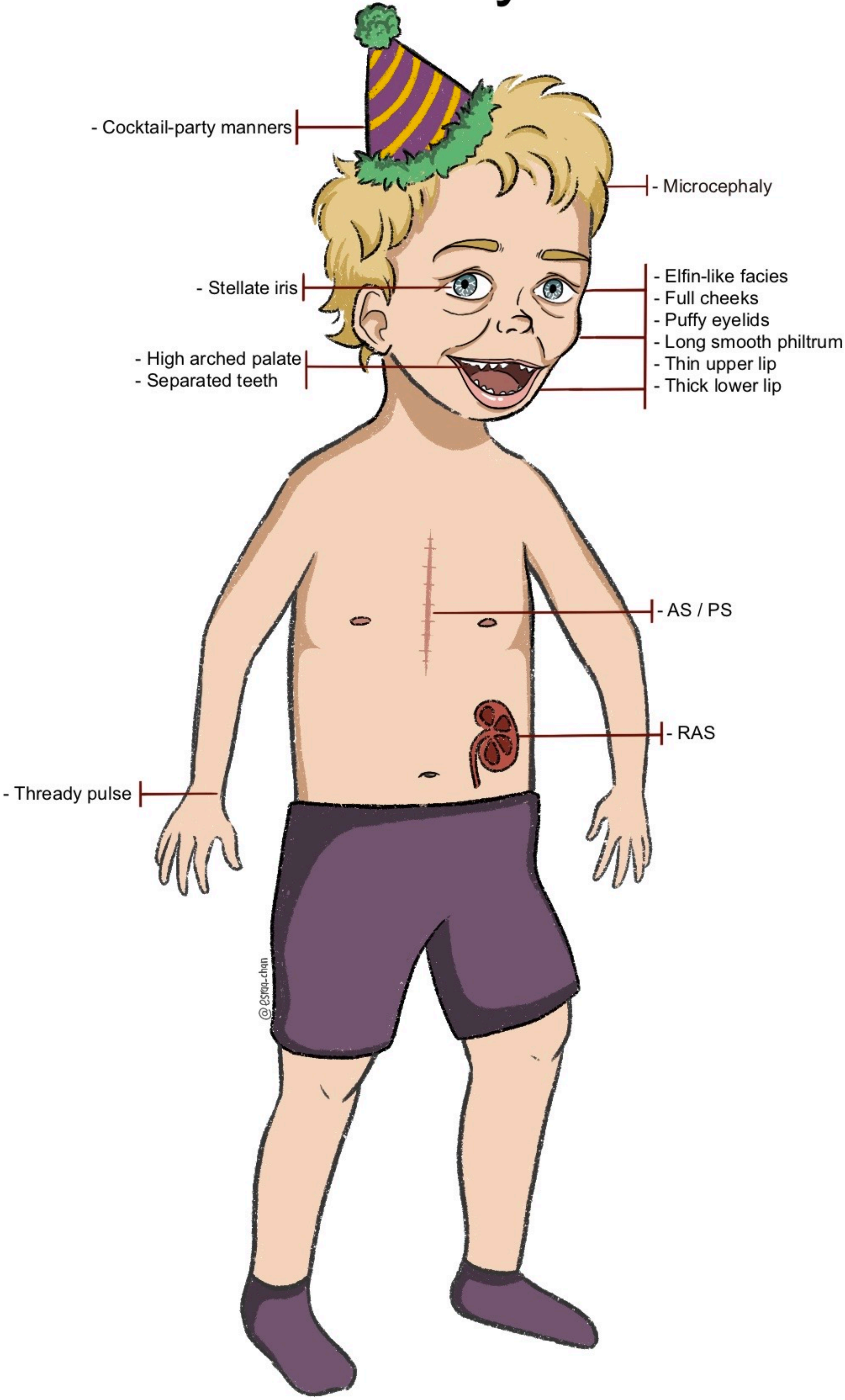
- Bruises

Williams Syndrome


- Cocktail-party manners
- Microcephaly
- Stellate iris
- Elfin-like facies
- Full cheeks
- Puffy eyelids
- Long smooth philtrum
- Thin upper lip
- Thick lower lip
- High arched palate
- Separated teeth
- AS / PS
- RAS
- Thready pulse
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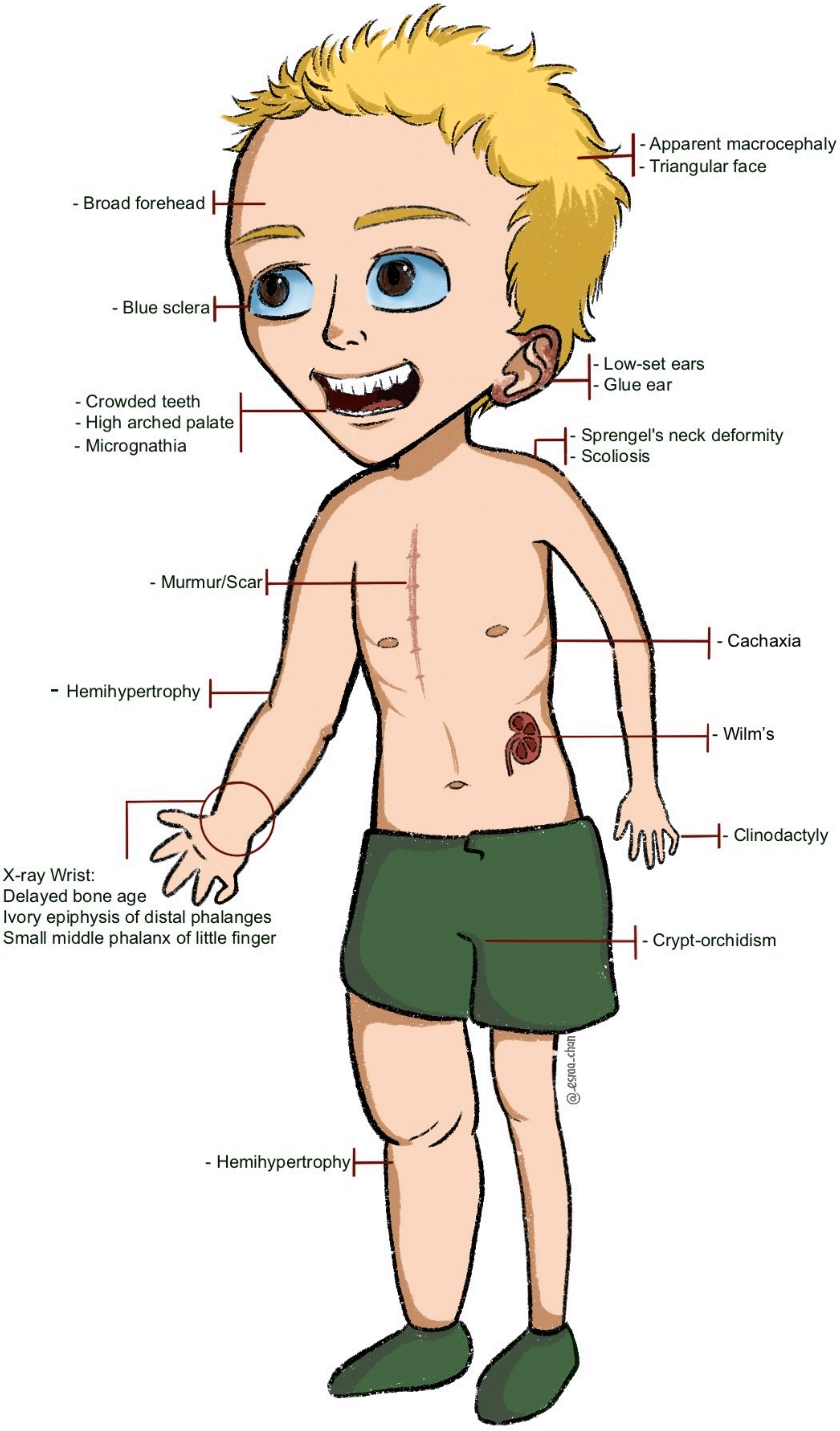
Russell-Silver Syndrome


- Apparent macrocephaly
- Triangular face
- Broad forehead
- Blue sclera
- Low-set ears
- Glue ear
- Crowded teeth
- High arched palate
- Micrognathia
- Sprengel's neck deformity
- Scoliosis
- Murmur/Scar
- Cachaxia
- Hemihypertrophy
- Wilm's
- Clinodactyly
X-ray Wrist:
Delayed bone age
Ivory epiphysis of distal phalanges
Small middle phalanx of little finger
- Crypt-orchidism
- Hemihypertrophy
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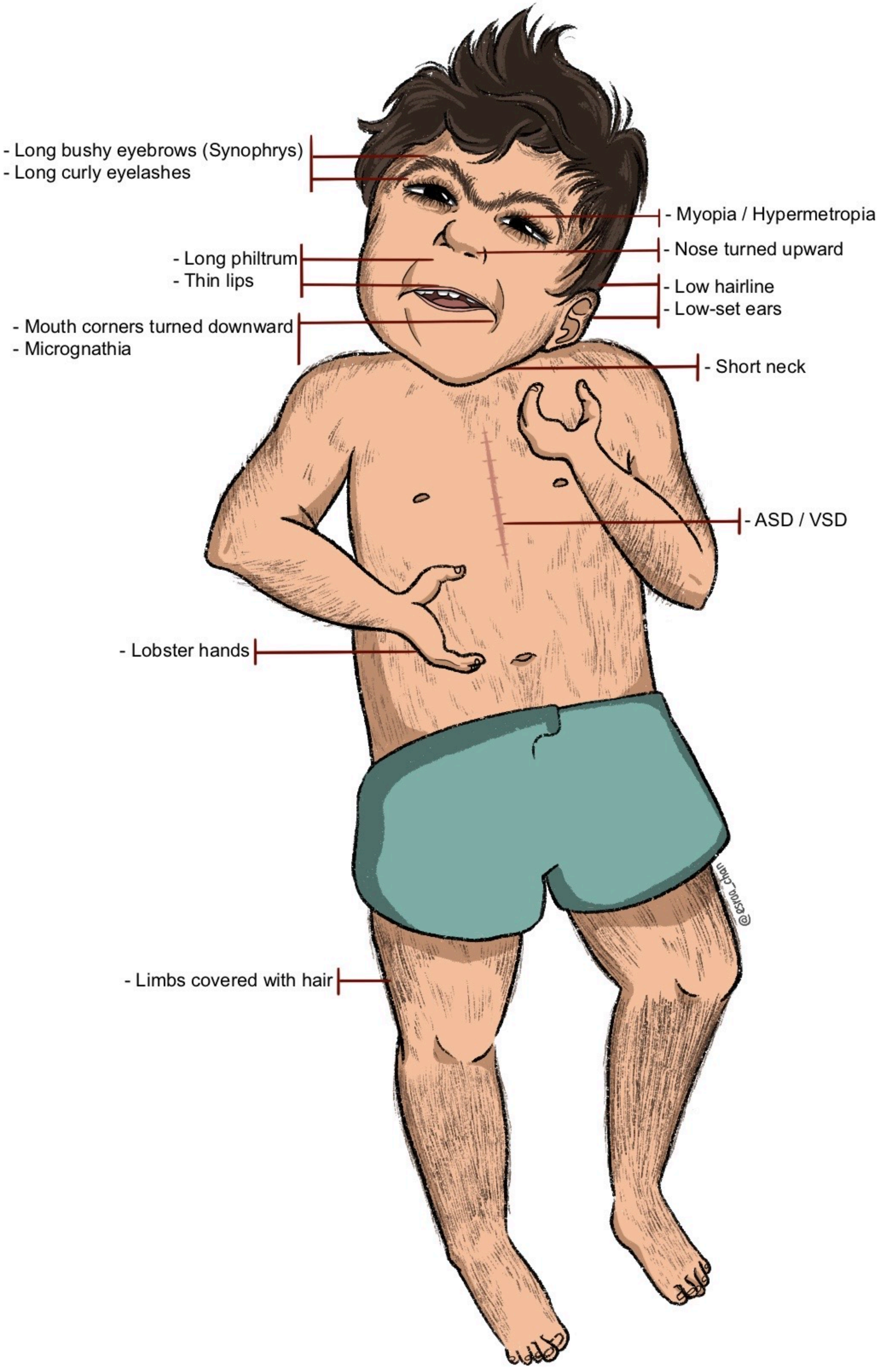
Cornelia de Lange Syndrome


- Long bushy eyebrows (Synophrys)
- Long curly eyelashes
- Myopia / Hypermetropia
- Long philtrum
- Thin lips
- Nose turned upward
- Low hairline
- Low-set ears
- Mouth corners turned downward
- Micrognathia
- Short neck
- ASD / VSD
- Lobster hands
- Limbs covered with hair
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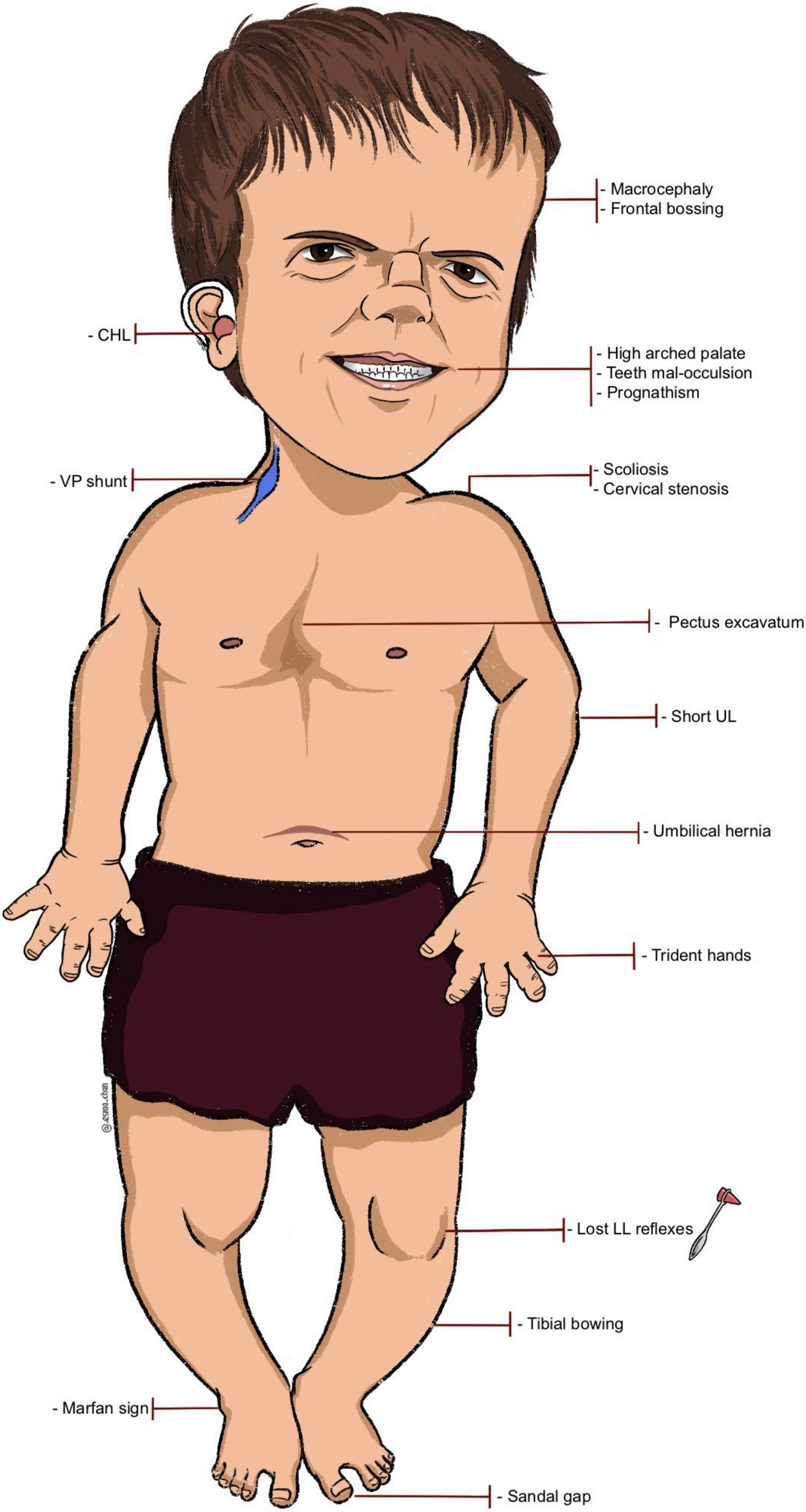
Achondroplasia


- Macrocephaly
- Frontal bossing
- CHL
- High arched palate
- Teeth mal-occulsion
- Prognathism
- VP shunt
- Scoliosis
- Cervical stenosis
- Pectus excavatum
- Short UL
- Umbilical hernia
- Trident hands
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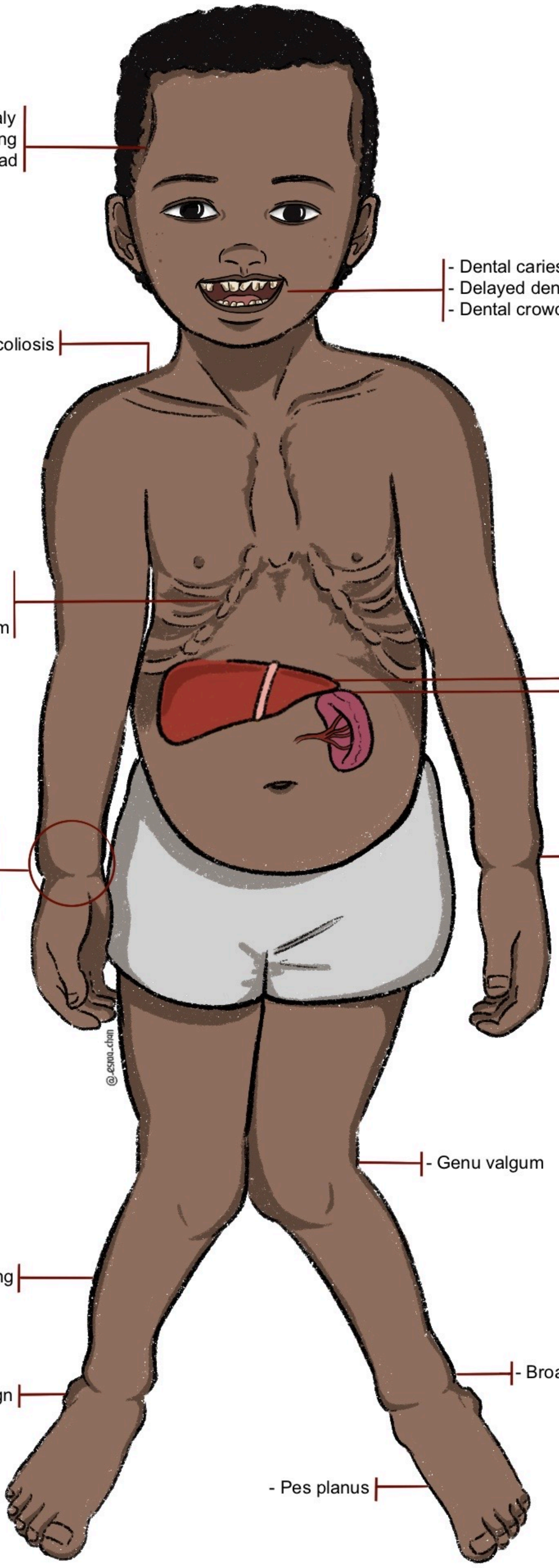
- Lost LL reflexes
- Tibial bowing
- Marfan sign
- Sandal gap

Rickets



- Dolichocephaly
- Frontal bossing
- Broad forehead

- Dental caries
- Delayed dentition
- Dental crowding

- Scoliosis

- Rosary beads
- Harrison's sulci
- Pectus carinatum

- Ptosis

Wrist X-ray:
- Cupping of end long bones
- Fraying of lone bones
- Widening of joint space
- Osteopenia
- Green-stick fracture

- Broadening of wrists

- Genu valgum

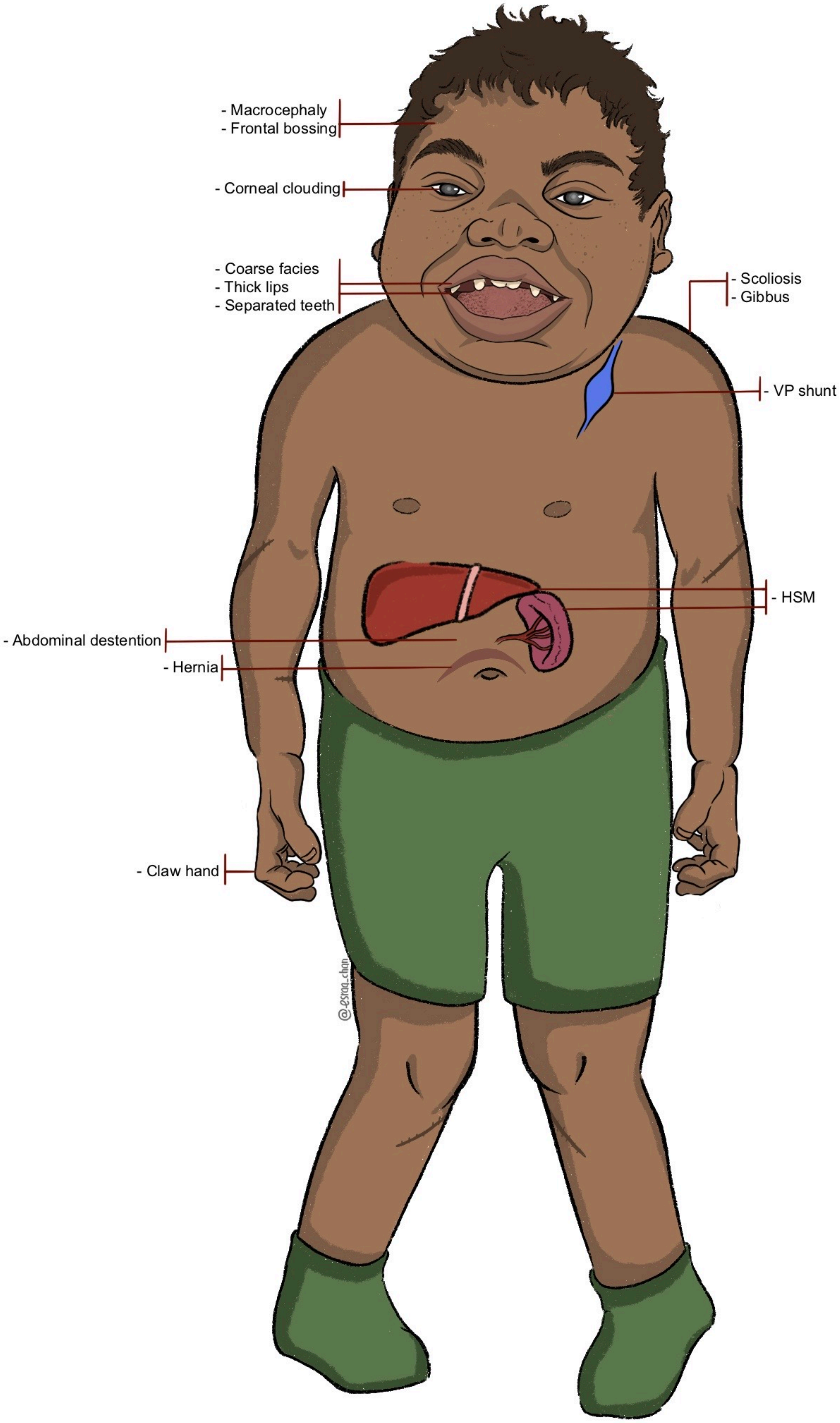
- Anterior tibial bowing

- Broadening of ankles

- Marfan sign

- Pes planus

Mucopolysaccharidosis


- Macrocephaly
- Frontal bossing
- Corneal clouding
- Coarse facies
- Thick lips
- Separated teeth
- Scoliosis
- Gibbus
- VP shunt
- HSM
- Abdominal destention
- Hernia
- Claw hand
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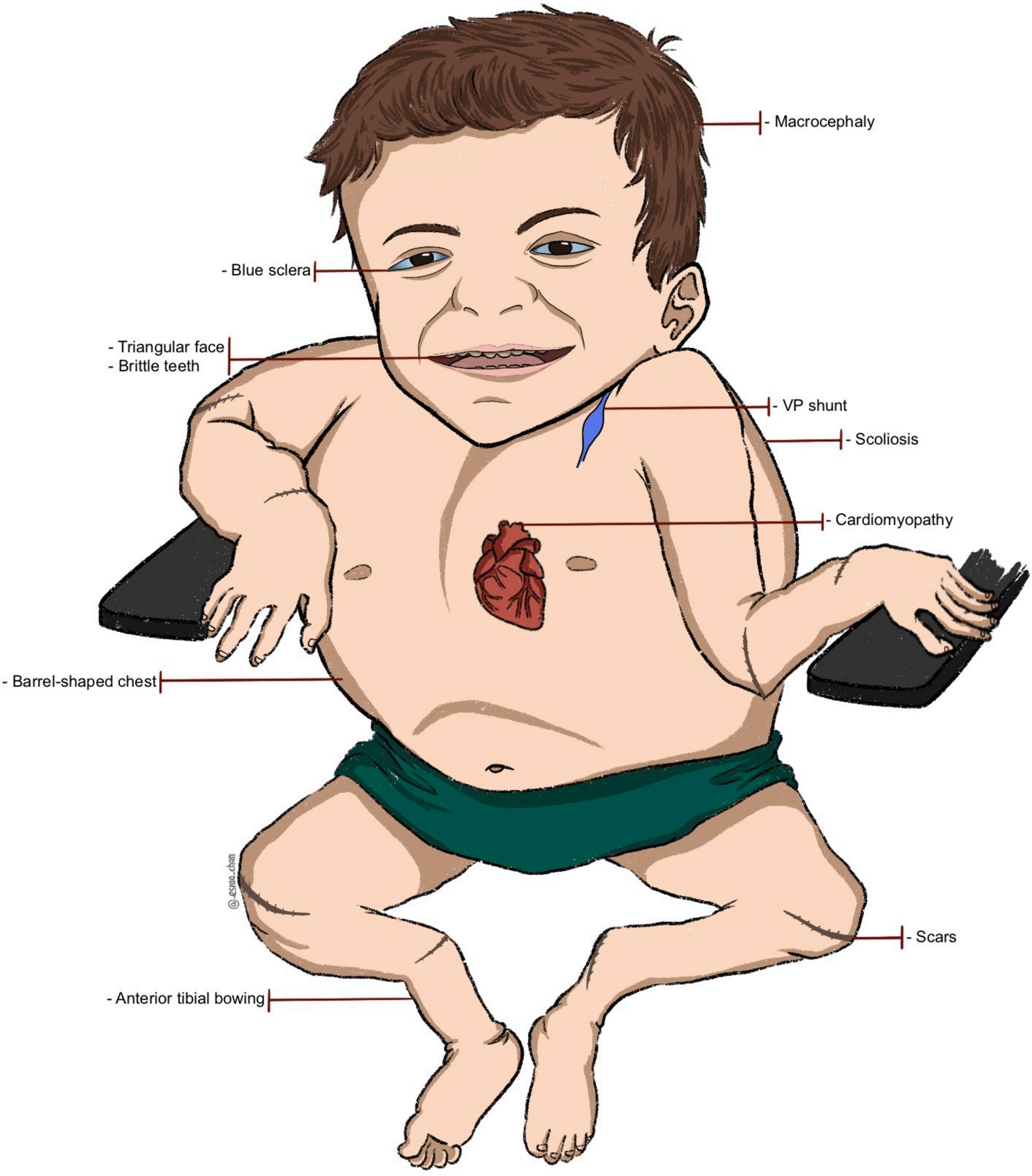
Osteogenesis Imperfecta


- Macrocephaly
- Blue sclera
- Triangular face
- Brittle teeth
- VP shunt
- Scoliosis
- Cardiomyopathy
- Barrel-shaped chest
- Scars
- Anterior tibial bowing
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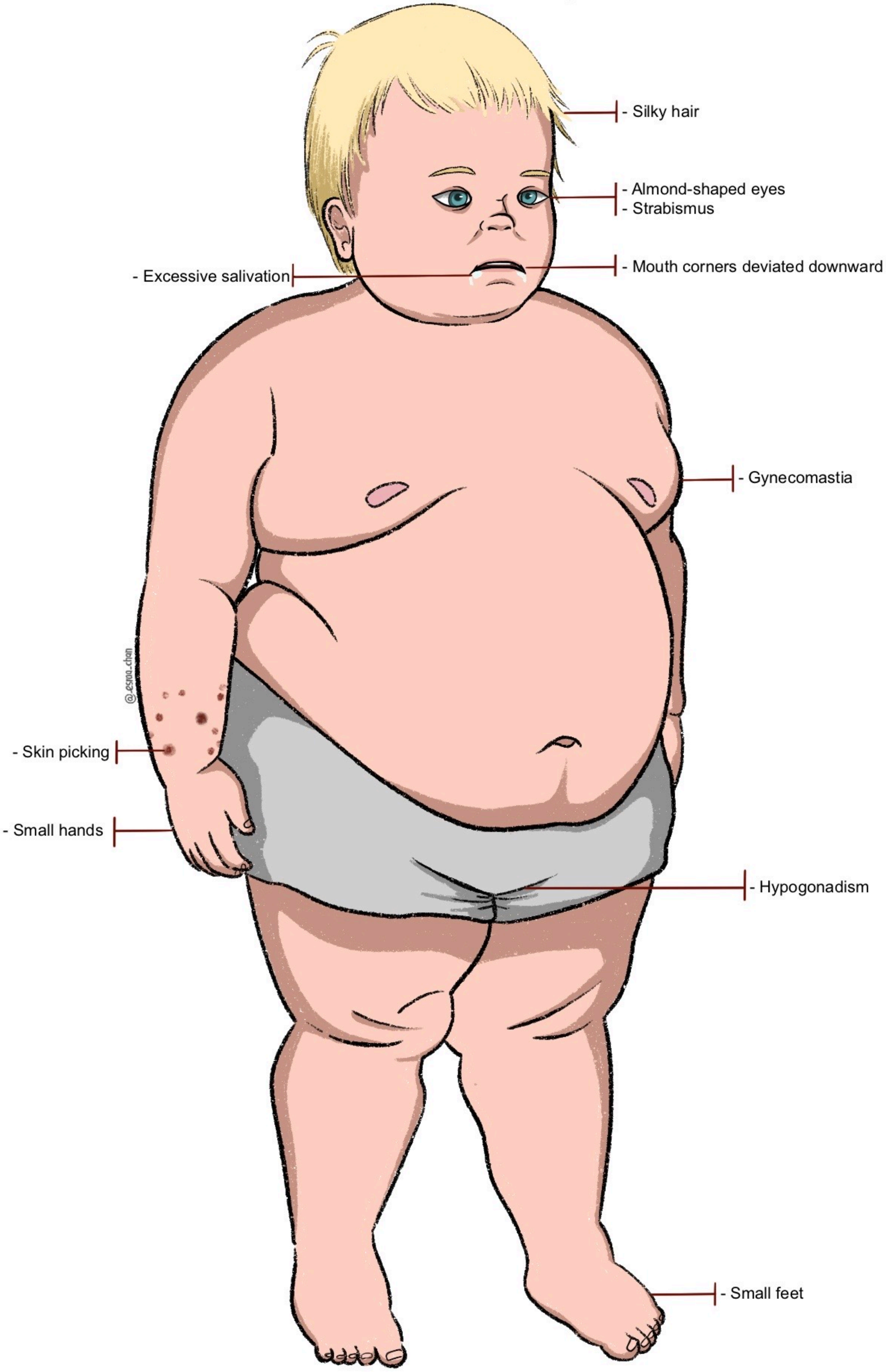
Prader-Willi Syndrome


- Silky hair
- Almond-shaped eyes
- Strabismus
- Excessive salivation
- Mouth corners deviated downward
- Gynecomastia
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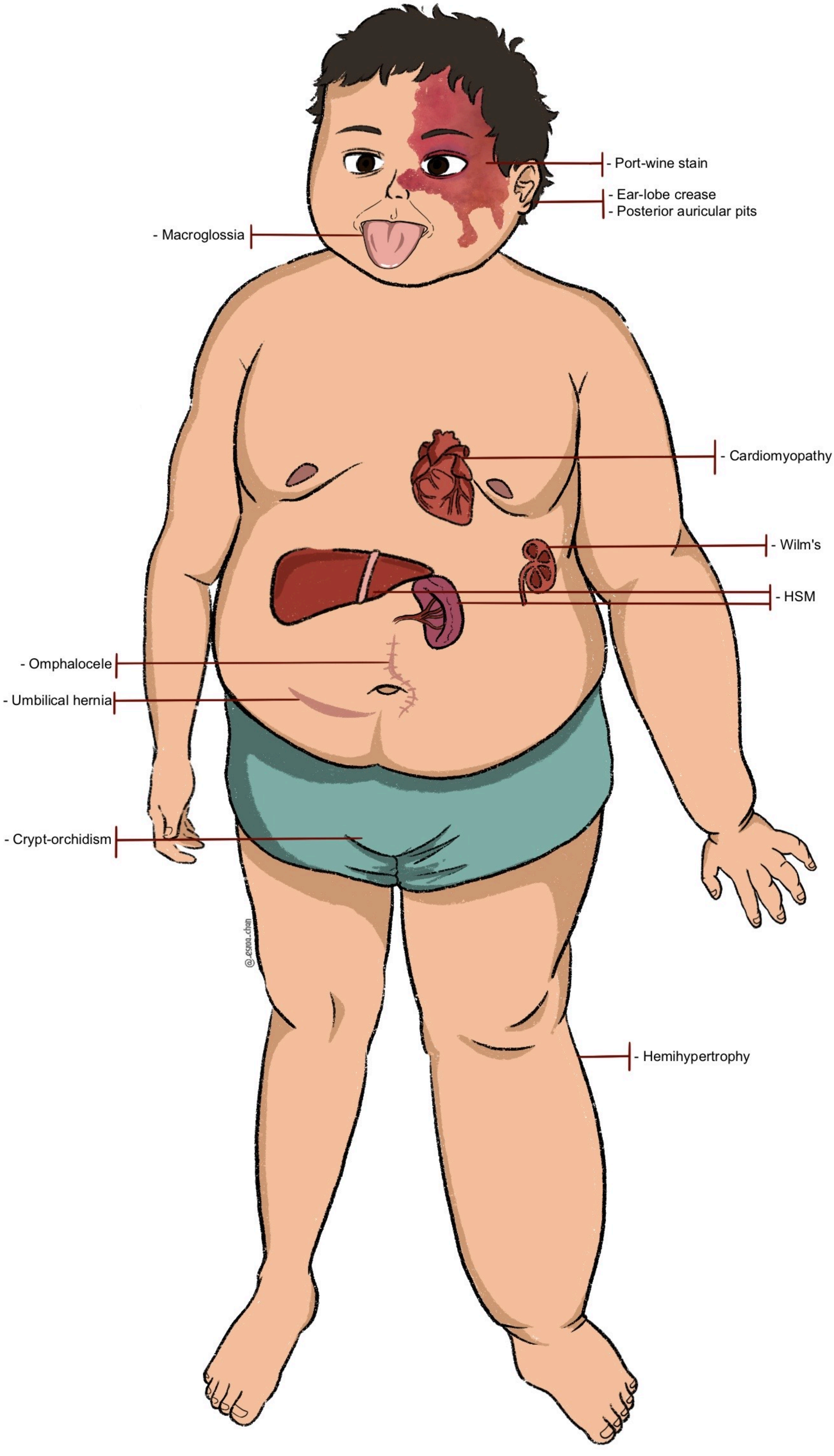
- Skin picking
- Small hands
- Hypogonadism
- Small feet

Beckwith-Wiedemann Syndrome


- Port-wine stain
- Ear-lobe crease
- Posterior auricular pits
- Macroglossia
- Cardiomyopathy
- Wilm's
- HSM
- Omphalocele
- Umbilical hernia
- Crypt-orchidism
- Hemihypertrophy
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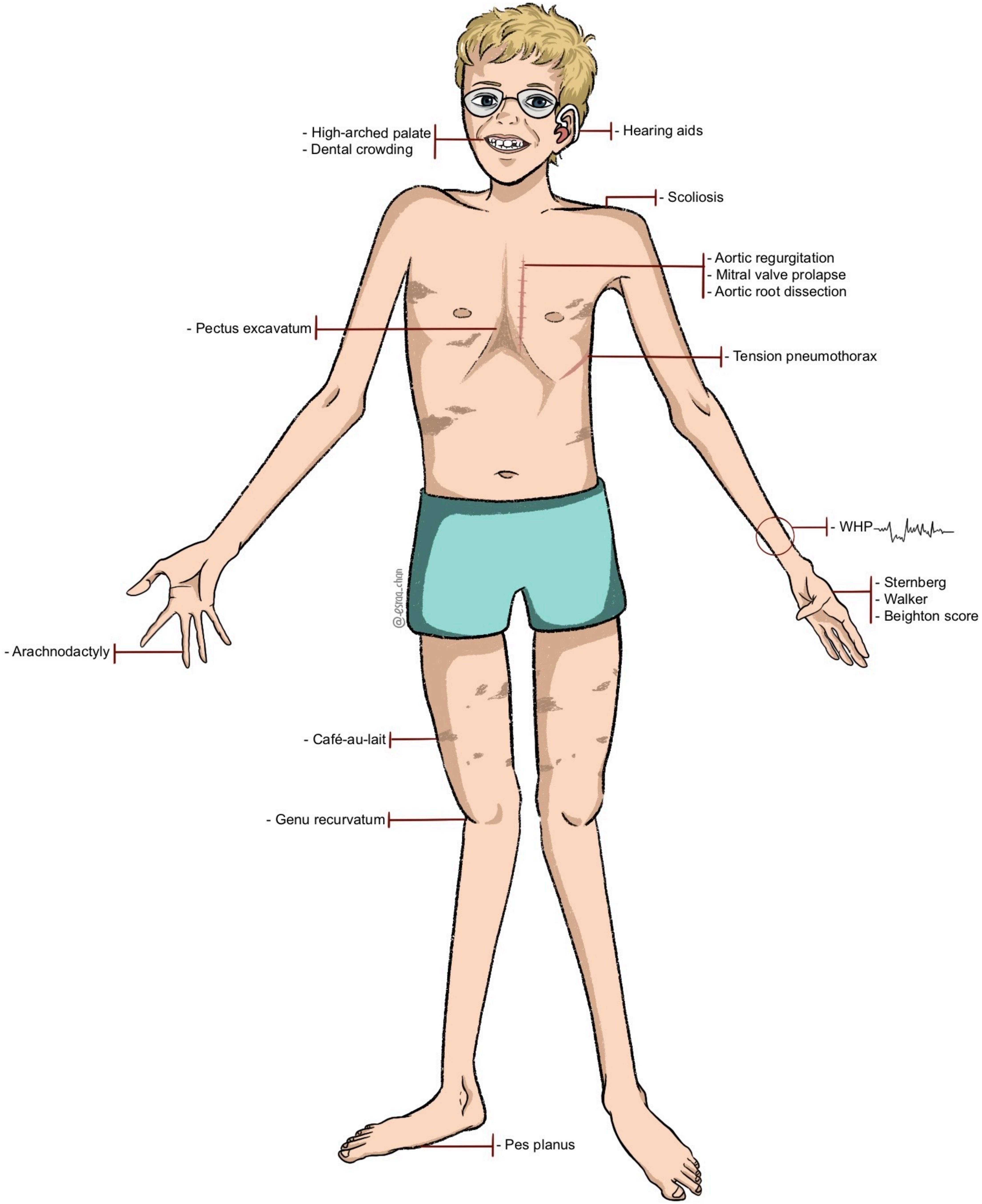
Marfan Syndrome


- High-arched palate
- Dental crowding
- Hearing aids
- Scoliosis
- Aortic regurgitation
- Mitral valve prolapse
- Aortic root dissection
- Pectus excavatum
- Tension pneumothorax
- WHP
- Sternberg
- Walker
- Beighton score
- Arachnodactyly
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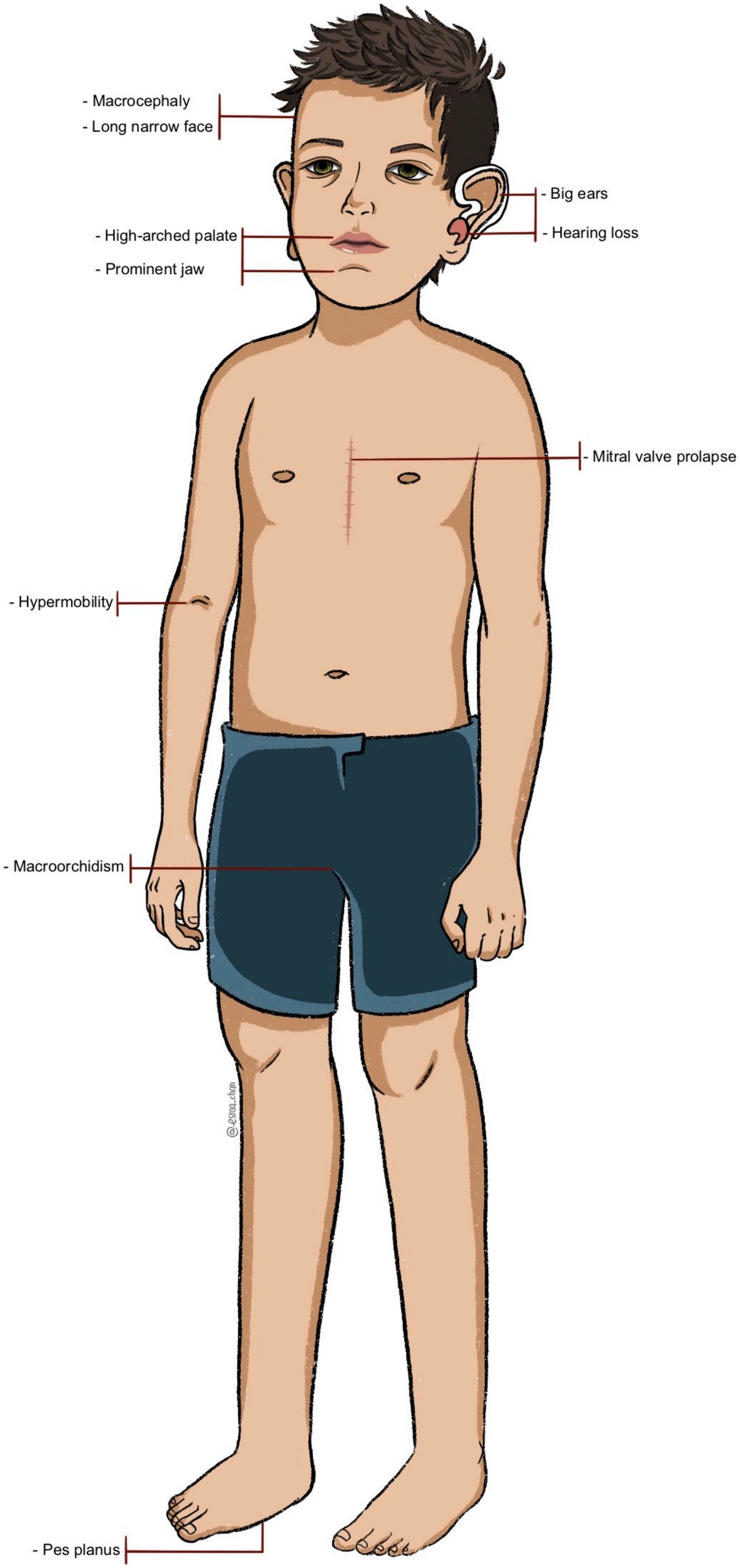
- Café-au-lait
- Genu recurvatum
- Pes planus

Fragile X Syndrome


- Macrocephaly
- Long narrow face
- Big ears
- Hearing loss
- High-arched palate
- Prominent jaw
- Mitral valve prolapse
- Hypermobility
- Macroorchidism
- Pes planus
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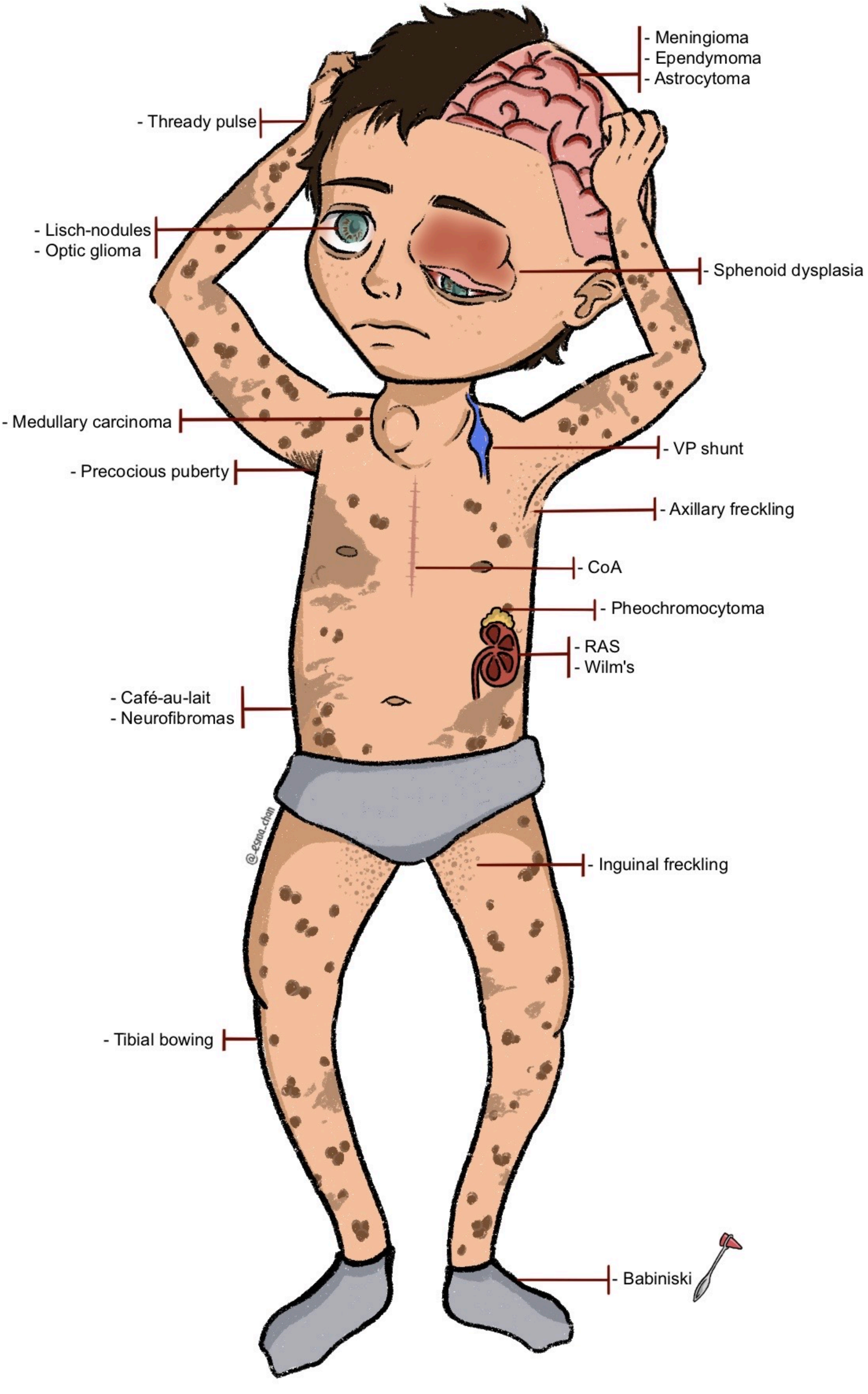
Neurofibromatosis Type 1


- Meningioma
- Ependymoma
- Astrocytoma
- Thready pulse
- Lisch-nodules
- Optic glioma
- Sphenoid dysplasia
- Medullary carcinoma
- VP shunt
- Precocious puberty
- Axillary freckling
- CoA
- Pheochromocytoma
- RAS
- Wilm's
- Café-au-lait
- Neurofibromas
- Inguinal freckling
- Tibial bowing
- Babiniski

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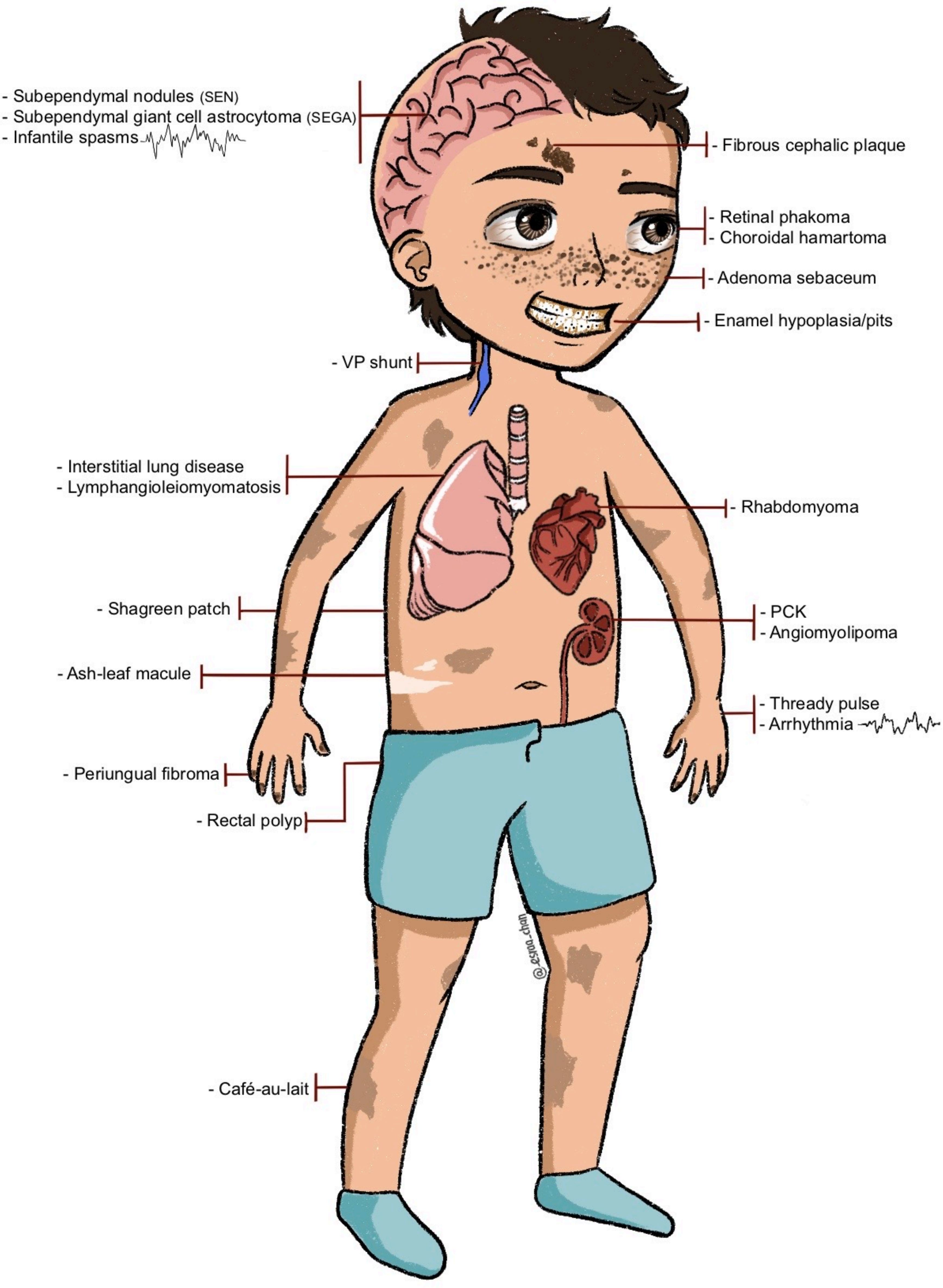
Tuberous Sclerosis


- Subependymal nodules (SEN)
- Subependymal giant cell astrocytoma (SEGA)
- Infantile spasms
- Fibrous cephalic plaque
- Retinal phakoma
- Choroidal hamartoma
- Adenoma sebaceum
- Enamel hypoplasia/pits
- VP shunt
- Interstitial lung disease
- Lymphangioleiomyomatosis
- Rhabdomyoma
- Shagreen patch
- PCK
- Angiomyolipoma
- Ash-leaf macule
- Thready pulse
- Arrhythmia
- Periungual fibroma
- Rectal polyp
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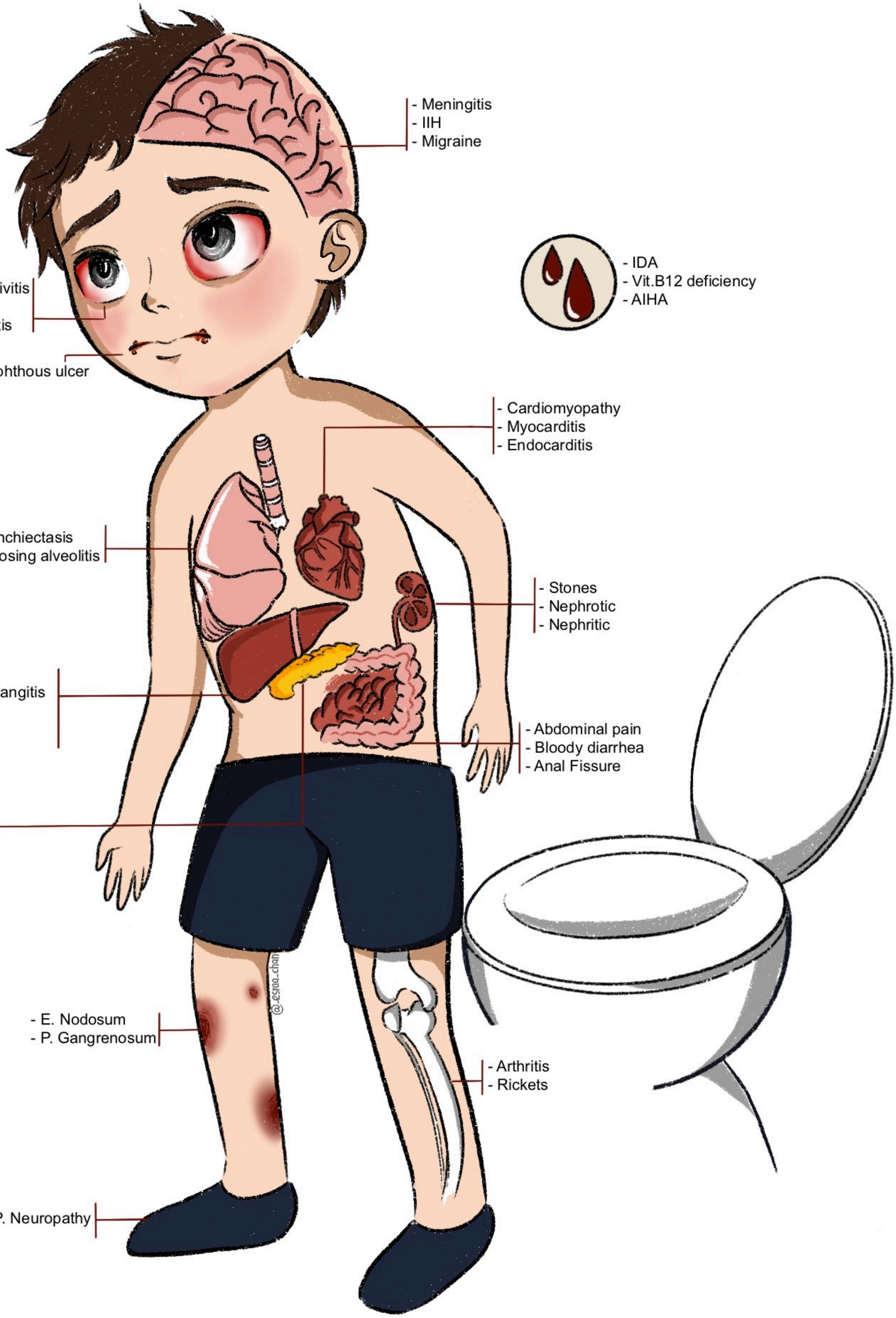
- Café-au-lait

Inflammatory Bowel Disease



- Meningitis
- IIH
- Migraine

- IDA
- Vit.B12 deficiency
- AIHA

- Conjunctivitis
- Uveitis
- Episcleritis

- Aphthous ulcer

- Cardiomyopathy
- Myocarditis
- Endocarditis

- Bronchiectasis
- Fibrosing alveolitis

- Stones
- Nephrotic
- Nephritic

- 1ry sclerosing cholangitis
- Cholelithiasis
- AI hepatitis

- Abdominal pain
- Bloody diarrhea
- Anal Fissure

- Pancreatitis

- E. Nodosum
- P. Gangrenosum

- Arthritis
- Rickets

- P. Neuropathy

Syndromes with blond hair or fair complexion

1- Albinism.

2- Phenylketonuria.

3- Homocystinuria.

4- Chediak Higashi syndrome.

5- Hermansky Pudlak syndrome.

6- Cystinosis.

7- Angelman syndrome.

8- Prader Willi syndrome.

9- Uncombable hair syndrome.

10- Richner Hanhart syndrome (tyrosinemia type Π).

11- Cartilage hair hypoplasia.

12- Vogt Koyanagi Harada syndrome.

13- Cross McKusick Breen syndrome.

14- Menkes (Kinky hair syndrome).

Syndromes with absent radius or limb defects

1- Fanconi anemia.

2- TAR syndrome (Thrombocytopenia with Absent Radius).

3- VATER association (Vertebral, Anal, TracheoEsophageal and Radial or Renal).

4- Holt Oram syndrome.

5- Robert's syndrome.

6- Edward's syndrome (trisomy 18).

7- Adams Oliver syndrome.

Syndromes with blue sclera

1- Marfan's syndrome.

2- Phenylketonuria.

3- Homocystinuria.

4- Type I AR Pseudoxanthoma elasticum.

5- Type Π AD Pseudoxanthoma elasticum.

6- Turner syndrome.

7- Osteogenesis imperfecta (Van der Hove syndrome).

8- Hallerman Streiff syndrome.

9- May be in iron deficiency anemia.

10- Ehlers Danlos syndrome.

11- Russel Silver syndrome.

12- Pyknodysostosis.

13- Diamond Blackfan anemia.

14- Alkaptonuria

15- Loyes Dietz syndrome.

16- Hypophosphatasia.

17- Weaver syndrome.

18- May be in Waardenburg syndrome (but the most common is heterochromia iridis).

Syndromes with café au lait macules

1- Neurofibromatosis (especially type I or Von Recklinghousen disease).

2- Tuberous sclerosis (Bourneville disease).

3- McCune-Albright syndrome.

4-Russell-Silver syndrome.

5- Ataxia telangiectasia.

6- Fanconi anemia.

7- Bloom syndrome.

8- Gaucher disease.

9- Basal cell nevus syndrome (Gorlin Goltz syndrome).

10- Chédiak-Higashi syndrome.

11- Hunter syndrome.

12- Maffucci syndrome (Hemangiomatosis with enchondromatosis).

13- Multiple mucosal neuroma syndrome (Multiple endocrine neoplasia type Π B).

14- Watson syndrome.

15- Proteus syndrome.

16- Ring chromosome syndrome.

17- Jaffe Campanacci syndrome.

18- Phakomatosis pigmentovascularis.

19- Juvenile xanthogranuloma.

20- Turner syndrome.

21- Halal-Setton-Wang syndrome.

22- Connective tissue dysplasia, Spellacy type.

Syndromes with polydactyly

1- Carpenter syndrome.

2- Ellis van Creveld syndrome.

3- Meckel Gruber syndrome.

4- Patau syndrome (Trisomy 13).

5- Rubinstein-Taybi syndrome.

6- Orofaciodigital syndrome.

7- Carpenter syndrome (Acrocephalopolysyndactyly).

8- Smith Lemli Opitz type I (classic form).

9- Saldino Noonan syndrome (short rib polydactyly type I).

10- Majewski syndrome (short rib polydactyly type Π).

11- Verma Naumoff syndrome (short rib polydactyly type Ш).

12- Beemer Langer syndrome (short rib polydactyly type IV).

13- Pallister Hall syndrome.

14- Greig cephalopolysyndactyly.

15- Orofaciodigital (Mohr) syndrome.

16- Impossible syndrome (Chondrodysplasia situs inversus imperforate anus polydactyly).

17- Sakati Nyhan Tisdale Syndrome.

18- Rieger's syndrome.

Syndromes with syndactyly

1- Apert syndrome (acrocephalosyndactyly).

2- Carpenter syndrome.

3- Cornelia de Langes syndrome.

4- Holt Oram syndrome.

5- Carpenter syndrome.

6- Down syndrome (trisomy 21).

7- Fetal hydantoin syndrome.

8- Laurence Moon Biedl syndrome.

9- Fanconi anemia.

10- Patau syndrome (trisomy 13).

11- Edward's syndrome (trisomy 18).

12- Poland syndrome.

13- Saethre Chotzen syndrome.

14- 13q- syndrome.

15- Russell Silver syndrome.

16- Smith Lemli Opitz type Π (acrodysgenital syndrome).

17- Greig cephalopolysyndactyly.

18- Orofaciodigital syndrome (Mohr syndrome).

19- Fraser Francois syndrome (Meyer Schwickerath's syndrome).

20- Timothy syndrome.

21- Oculodentodigital syndrome.

22- Sakati Nyhan Tisdale Syndrome.

23- Lenz Majewski syndrome.

24- Cri du Chat syndrome (5p- syndrome).

Common syndromes with arachnodactyly

1- Marfan syndrome.

2- Homocystinuria.

3- MASS phenotype.

4- Klinefelter syndrome.

5- Schprintzen Goldberg syndrome (craniosynostosis arachnodactyly syndrome).

6- Mucosal neuroma syndrome (MEN type Π B).

7- Beals syndrome (Congenital contractural arachnodactyly, Beals Hecht syndrome).

8- Rieger's syndrome.

9- Marden Walker syndrome.

10- Spondyloepimetaphyseal dysplasia.

11- Stickler Syndrome.

Common syndromes with clinodactyly

1- Down's syndrome.

2- Klinefelter syndrome and its variants.

3- Cornelia de Lange syndrome.

4- Russell Silver syndrome.

5- Carpenter syndrome.

6- Proteus syndrome.

7- Otopalatodigital syndrome.

8- Alpha thalassemia mental retardation X linked (ATR X syndrome).

9- Robinow syndrome.

10- Robert's syndrome.

11- Seckel syndrome.

12- Saethre Chotzen syndrome.

13- Weaver syndrome.

14- Jansen type metaphyseal chondrodysplasia.

15- 13q- syndrome.

Syndromes with fetal overgrowth

1- Infant of diabetic mother.

2- Beckwith Wiedemann syndrome.

3- Weaver syndrome.

4- Sotos syndrome.

5- Simpson Golabi Behmel overgrowth syndrome.

6- Nesidioblastosis.

7- MOMO syndrome.

Syndromes with craniosynostosis

1- Carpenter syndrome.
2- Apert syndrome.
3- Crouzon syndrome.
4- Saethre Chotzen syndrome.
5- Pfeiffer syndrome.
6- Shprintzen Goldberg syndrome (craniosynostosis arachnodactyly syndrome).
7- Antley Bixler syndrome.
8- Jackson Weiss syndrome.
9- Muenke Syndrome.
10- SCARF syndrome (Skeletal defects, Cutis laxa Craniostenosis, Abnormal genitals, Retardation and Facial dysmorphism).
11- Thanatophoric dysplasia.
12- Loyes Dietz syndrome.
13- Crouzonodermatoskeletal syndrome.
14- Potocki Shaffer syndrome.

Syndromes with macrocephaly

1- Rickets.
2- Chronic hemolytic anemia.

3- Achondroplasia.

4- Osteogenesis imperfecta.

5- Mucopolysaccharidosis.

6- Canavan disease.

7- Alexander disease.

8- GM1 gangliosidosis (infantile type).

9- Tay Sachs disease.

10- Sandhoff disease.

11- Pseudo Hurler polydystrophy.

12- Klippel Trenaunay Weber syndrome.

13- Kniest syndrome.

14- Lenz Majewski syndrome.

15- Zori Stalker Williams syndrome.

16- Cardiofaciocutaneous Syndrome.

17- MOMO syndrome.

18- Sotos syndrome.

19- Gorlin syndrome.

20- Glutaric aciduria type 1.

Syndromes with coarse facial features

1- Hypothyroidism (cretinism).

2- Mucopolysaccharidosis.

3- GM 1 gangliosidosis (infantile type).

4- Sialidosis type Π.

5- Pseudo Hurler polydystrophy.

6- Tay Sachs disease.

7- Patau syndrome.

8- Job Buckley syndrome (hyper IgE syndrome).

9- Pallister Killian syndrome.

10- Costello syndrome.

11- Klinefelter variants.

12- Cri du Chat syndrome.

13- Smith Lemli Opitz syndrome.

Syndromes with Aplasia cutis congenita (Absent skin).

1- Trisomy 13.

2- Adams Oliver syndrome.

3- Johanson Blizzard syndrome.

4- Bart’s syndrome.

5- Goltz syndrome.

Syndromes with obesity

1- Cushing syndrome.

2- Alström Hallgren syndrome.

3- Laurence Moon Biedl syndrome (Bardet Biedl syndrome).

4- Cohen syndrome.

5- Prader Willi syndrome.

6- Frolich syndrome.

7- Hereditary Albright osteodystrophy.

8- hypothyroidism.

9- Carpenter syndrome.

10- Turner syndrome.

11- 9 q 34 deletion syndrome.

12- Down's syndrome.

13- Stein Leventhal syndrome (polycystic ovary syndrome).

14- MOMO syndrome.

15- Urban Rogers Meyer syndrome.

Syndromes with accelerated aging

1- Hutchinson Gilford Progeria syndrome.

2- Werner syndrome.

3- Cockayne syndrome (Weber Cockayne syndrome or Neill Dingwall Syndrome).

4- Neonatal progeroid syndrome (Wiedemann Rautenstrauch syndrome).

5- Gottron's syndrome (acrogeria).

6- Gerodermia osteodysplastica (GO).

7- DeBarsy syndrome.

Syndromes with redundant skin folds

1- Cutis laxa congenita.

2- Costello syndrome.

3- Noonan syndrome (over the posterior part of the neck).

4- Turner syndrome (over the posterior part of the neck).

5- Down's syndrome (over the posterior part of the neck).

6- Klippel Feil syndrome (over the posterior part of the neck).

7- Ehlers Danlos syndrome.

8- Pseudoxanthoma elasticum.

9- Short limbed dwarfism.

10- DeBarsy syndrome.

11- Lenz Majewski syndrome.

12- SCARF syndrome.

13- Hyperostotic dwarfism.

14- Wrinkly skin syndrome.

15- Cartilage hair hypoplasia.

16- Edward's syndrome.

17- 1p36 monosomy.

Syndromes with lens dislocation or ectopia lentis

1- Marfan syndrome.

2- Homocystinuria.

3- Sulfite oxidase deficiency.

4- Weill Marchesani syndrome.

5- Sturge Weber syndrome.

6- Klippel Feil syndrome.

7- Oxycephaly.

8- Treacher Collins syndrome (mandibulofacial dysostosis).

9- Zazam Sheriff Phillips syndrome.

Syndromes with lentiginosis

1- Addison disease.

2- Lentiginosis profusa.

3- Carney complex or LAMB syndrome (Lentiginosis, Atrial myxomas, Mucocutaneous myxomas and Blue nevi). Pituitary, thyroid, testicular tumors, pigmented melanotic schwannomas and Primary pigmented nodular adrenocortical disease are common associations. It is an AR disorder.

4- LEOPARD syndrome (Lentiginosis, Electrocardiographic abnormalities, Ocular hypertelorism, Pulmonary stenosis, Abnormal genitals, growth Retardation and Deafness).

5- Peutz-Jeghers syndrome.

6- Laugier Hunziker syndrome.

Skeletal dysplasias with renal affection

1- Lethal conditions:

- Saldino Noonan syndrome (short rib polydactyly type I).
-Majewski syndrome (short rib polydactyly type Π).

2- Non lethal conditions:

- Asphyxiating thorathic dysplasia (Jeune syndrome).

- Saldino Mainzer syndrome (dysplasia, retinitis pigmentosa and nephropathy).
- Robinow syndrome.
- Nail Patella syndrome.

Syndromes with rib dysplasias

1- Saldino Noonan syndrome (short rib polydactyly type I).
2- Majewski syndrome (short rib polydactyly type Π).
3- Verma Naumoff syndrome (short rib polydactyly type Ш).
4- Beemer Langer syndrome (short rib polydactyly type IV).
5- Ellis van Creveld syndrome.
6- Asphyxiating thorathic dysplasia (Jeune syndrome).
7- Cartilage hair hypoplasia.
8- Adenosine deaminase deficiency.
9- Thanatophoric dysplasia.
10- Achondroplasia.
11- Achondrogenesis: type I (Parenti Fraccaro) and type Π (Langer Saldino).
12- Jarcho Levin Syndrome.
13- Gorlin syndrome.
14- Patau syndrome.
15- Shwachman Diamond syndrome.

Syndromes with bronchiectasis

1- Williams-Campbell syndrome: in which there is an absence of annular bronchial cartilage.

2- Marnier-Kuhn syndrome (congenital tracheobronchomegaly).

3- Right middle lobe syndrome or Brock's syndrome (chronic extrinsic compression of right middle lobe bronchus by hilar lymph nodes).

4- Yellow nail syndrome (pleural effusion, lymphedema, discolored nails).

5- Kartagner's syndrome (bronchiectasis, chronic sinusitis, dextrocardia and situs inversus, infertility and azoospermia in males).

6- Young's syndrome (chronic sinusitis, dextrocardia, bronchiectasis, azoospermia and may be finger clubbing).

Syndromes with chromosomal instability

1- Ataxia telangiectasia.

2- Fanconi anemia.

3- Bloom syndrome.

4- Cockayne syndrome.

5- Xeroderma pigmentosa.

6- Dyskeratosis congenita.

7- ICF syndrome (Immunodeficiency, Centromeric instability and Facial dysmorphism).

8- Nijmegen breakage syndrome.
9- Seckel syndrome (Bird headed dwarfism).
10- Dysplastic nevus syndrome.
11- Rothmund Thompson syndrome.
12- Werner syndrome.
13- Robert's syndrome.

Syndromes associated with deafness

1- Usher (Hallgren) syndrome.
2- Waardenburg syndrome.
3- Branchio otorenal syndrome (BOR).
4- Barakat (HDR) syndrome.
5- Osteogenesis imperfecta.
6- Alport syndrome.
7- LEOPARD syndrome.
8- MERRF.
9- MELAS mutation.
10- Kearns Sayre syndrome.
11- Langerhans cell histeocytosis.
12- Osteopetrosis.
13- Pendred syndrome.
14- Jervell and Lange-Nielsen syndrome.
15- Norrie disease.
16- Otopalatodigital syndrome.
17- Patau syndrome.

18- Edward syndrome.

19- Down syndrome.

20- Turner syndrome.

21- Klippel Feil syndrome.

22- Alstrom Hallgren syndrome.

23- Neurofibromatosis.

24- Hurler-Hunter syndrome.

25- Treacher Collins syndrome.

26- Pierre Robin syndrome.

27- Stickler syndrome (hereditary osteoarthroophthalmopathy).

28- Apert Syndrome.

29- Crouzon Syndrome.

30- Pfeiffer syndrome.

31- Ectrodactyly ectodermal dysplasia cleft syndrome.

32- Saethre Chotzen Syndrome.

33- Shprintzen velocardiofacial syndrome.

34- Hemifacial microstomia.

35-STORCH syndrome.

36- Nager syndrome.

37- Flynn Aird syndrome.

38- Keutel syndrome.

39- Cogan syndrome.

40- DIDMOAD syndrome (Wolfram syndrome).

41- Refsum's disease.

42- Goldenhar syndrome (Oculoauriculovertebral spectrum).

43- Syndrome of Blepharophimosis, camptodactyly, short stature, metal retardation and inner ear hearing impairment.

44- Wildervanck syndrome (Cervico oculo acoustic, COA).

45- Orofaciodigital syndrome (Mohr syndrome, OFD).

46- ABCD syndrome.

47- Johanson Blizzard syndrome.

48- KID syndrome.

49- 1p36 deletion syndrome.

50- Woodhouse Sakati syndrome.

51- Kniest syndrome.

52- Renal tubular acidosis proximal type.

Syndromes with periodic fever

1- Familial Mediterranean Fever.

2-Tumor necrosis factor associated periodic syndrome (TRAPS).

3- Hyper IgD Syndrome.

4- Marshal syndrome or PFAPA (Periodic Fever, Aphthus stomatitis, Pharyngitis, Adenitis).

5- Mukle Wells syndrome.

6- Familial cold urticaria.

7- CINCA (Chronic Infantile Neurological Cutaneous and Articular disease).

8- PAPA (Pyogenic Arthritis, Pyoderma gangrenosum, Acne).

9- Blau syndrome (early onset granulomatous arthritis, uveitis, skin rash and flexion contracture of fingers).

Syndromes with long Q-T on ECG

1- Romano Ward syndrome (AD).
2- Jervell and Lange-Nielsen syndrome (AR, associated with deafness).
3- Timothy syndrome (AD).
4- Andersen Tawil syndrome (AD).
5- LEOPARD syndrome.

Syndromes associated with sudden infant death

1- Romano Ward syndrome.
2- Jervell and Lange-Nielsen syndrome.
3- Brugada syndrome.
4- Wolff-Parkinson-White syndrome.
5- Timothy syndrome.

Syndromes with giant platelets

1- Bernard Soulier syndrome.
2- Alport syndrome.
3- May Hegglin anomaly.

4- Sebastian syndrome.

5- Epstein syndrome.

6- Fechtner syndrome.

Syndromes with increased incidence of malignancy than normal

Hematological syndromes:

1- Fanconi anemia: leukemia, myelodysplastic syndrome, liver tumors, rare head and neck tumors, gastrointestinal and genitourinary cancer.

2- Diamond Blackfan anemia: acute leukemia (usually myeloid) and myelodysplasia. Solid tumor malignancies also have been reported, in particular osteosarcoma.

3- Paroxysmal nocturnal hemoglobinuria (PNH or Marchiafava Micheli syndrome: leukemia.

4- Polycythemia rubra vera: myelofibrosis or acute leukemia.

5- Seckel syndrome.

6- Sickle cell trait: renal medullary carcinoma.

7- Schwachman Diamond syndrome: leukemia.

8- Hemochromatosis: hepatocellular carcinoma.

9- Amegakaryocytic thrombocytopenia: leukemia.

Chromosomal syndromes:

1- Turner syndrome: gonadoblastoma.

2- Noonan syndrome: acute lymphoblastic leukemia, chronic myelomonocytic leukemia, Schwannoma and myelodysplasia.

3- Klinefelter syndrome: breast cancer, mediastinal germ cell tumors, lymphoma, leukemia and other hematologic tumors.

4- Down syndrome: lymphoid, non lymphoid tumors and megakaryocytic leukemia.

5- 11P- with sporadic aniridia: wilm's tumor.

6- Trisomy 8: Preleukemia.

7- 13q- syndrome: Retinoblastoma, sarcoma.

8-Monosmy 5 and 7: myelodysplastic syndromes.

Chromosomal instability syndromes:

1- Ataxia telangiectasia: Lymphoma, leukemia.

2- Xeroderma pigmentosa: basal, squamous cell skin cancers, melanoma and leukemia.

3- Bloom syndrome: Leukemia, lymphoma and solid tumors.

4- Rothmund Thomson syndrome: squamous cell carcinoma, osteosarcoma.

5- Cockayne syndrome.

6- Nijmegen breakage syndrome.

Neurocutaneous syndromes:

1- Neurofibromatosis I: neurofibroma, optic glioma, acoustic neuroma, astrocytoma, meningioma, pheochromocytoma and sarcoma.

2- Neurofibromatosis Π: bilateral acoustic neuromas, meningioma.

3- Von Hipple Lindau disease: Hemangioblastoma of the cerebellum and retina, pheochromocytoma, renal cell carcinoma.

4- Tuberous sclerosis: Fibroangiomatous nevi, myocardial rhabdomyoma.

Endocrinal syndromes:

1- Multiple endocrine neoplasia type I (MEN type I or Wermer syndrome): Parathyroid adenoma, pancreatic islet tumor, pituitary adenoma, carcenoid.

2- Multiple endocrine neoplasia type Π A (MEN type Π A or Sipple syndrome): Medullary carcinoma of the thyroid, hyperparathyroidism, and pheochromocytoma.

3- Multiple endocrine neoplasia type Π B (MEN type Π B or mucosal neuroma syndrome): Mucosal neuroma, pheochromocytoma, medullary thyroid carcinoma.

Metabolic syndromes:

1- Tyrosinemia: hepatocellular carcinoma.

2- Galactosemia: hepatocellular carcinoma.

3- Von Gierke disease: hepatocellular carcinoma.

Immunodeficiency syndromes:

1- X linked agammaglobulinemia (Bruton disease): Lymphoma, leukemia.

2- Common variable immunodeficiency: lymphoma, leukemia.

3- X linked lymphoproliferative disease (Duncan disease): lymphoma.

4- Severe combined immunodeficiency: leukemia, lymphoma.

5- Wisckot Aldrich syndrome (WAS): Lymphoma, leukemia.

6- Chediak Higashi syndrome: lymphoma.

Other syndromes:

1- Turcot's syndrome: colonic cancer, osteomas (mainly mandibular, fibromas, desmoid tumors and medulloblastoma.

2- Gardner syndrome: adenocarcinoma of the colon, breast and thyroid carcinoma and dysplastic gangliocytoma of the cerebellum (Lhermitte-Duclos disease).

3- Denys Drash syndrome: wilm's tumor.

4- WAGR syndrome: wilm's tumor.

5- Beckwith Wiedemann syndrome: wilm's tumor, hepatoblastoma, adrenal carcinoma.

6- Bannayan Riley Ruvalcaba syndrome: thyroid, breast cancer, GIT cancer.

7- Carney complex (LAMB syndrome): cardiac and cutaneous myxomas, pituitary, thyroid, and testicular tumors, and pigmented melanotic schwannomas.

8- Class Ш histeocytosis: malignant histeocytosis, acute myeloid leukemia.

9- Immunoproliferative small intestinal disease (Mediterranean lymphoma): lymphoma.

10- Maffucci syndrome: chondrosarcoma, hemangiosarcoma.

11- Gorlin Goltz syndrome: basal cell carcinoma, medulloblastoma.

12- Hallerman Streiff syndrome: hypothalamic hamartoblastoma.

13- Male pseudohermaphroditism with undescended testis: seminoma, germ cell tumors.

14- Peutz-Jeghers syndrome: Gastrointestinal carcinoma, ovarian neoplasia.

15- Rendu-Osler-Weber syndrome (hereditary hemorrhagic telangiectasia): angioma.

16- Cancer family syndrome: Colonic, uterine carcinoma.

17- Li-Fraumeni syndrome: Bone, soft tissue sarcoma, breast carcinoma, astrocytoma.

18- Birt-Hogg-Dubé syndrome.

19- Jacobsen syndrome.

20- Rubenstein Taybi syndrome.

Common syndromes with cleft lip and/or cleft palate

N.B : More than 300 syndromes are associated with cleft lip and/or cleft palate. I will mention only the most common of them.

1- Van der Woude syndrome (familial dominant inheritance of cleft lip and/or cleft palate).

2- Patau syndrome.

3- Pierre Robin syndrome.

4- Treacher Collins syndrome.

5- Ellis Van Creveld syndrome.

6- Edward's syndrome .

7- Diastrophic dysplasia.

8- Shprintzen velocadiofacial syndrome.

9- CATCH 22 syndrome.

10- EEC syndrome.

11- Larsen syndrome.

12- Meckel Gruber syndrome.

13- Kniest syndrome.

14- Wolf Hirschhorn syndrome.

15- Otopalatodigital syndrome (OPD).

16- Waardenburg syndrome.

17- Stickler syndrome.

18- Apert syndrome.

19- 18P- syndrome.

20- 17p11.2 deletion (Smith Magenis) syndrome.

21- Loyes Dietz syndrome.

Syndromes associated with dental anomalies

1- Dentinogenesis imperfecta.

2- Amelogenesis imperfecta.

3- Ellis Van Creveld syndrome.

4- Ectodermal dysplasia.

5- Job Buckley (hyper IgE) syndrome.

6- Meyloperoxidase deficiency.

7- Cockayne syndrome.

8- Congenital syphilis.

9- Treacher Collins syndrome.

10- Rieger's syndrome.

11- Incontinentia pigmenti (Bloch Sulzberger syndrome).

12- Cleidocranial dysplasia.

13- Pierre Robin syndrome.

14- Papillon-Lefèvre syndrome.

15- Histiocytosis X.

16- Riga fede disease.

17- Oculodentodigital syndrome (ODD).

18- Flynn Aird syndrome.

19- Timothy syndrome.

20- Benjamin syndrome.

21- SHORT syndrome.

22- Lenz Majewski syndrome.

23- Rubenstein Taybi syndrome.

24- Cornelia de Lange syndrome.

Syndromes associated with retinitis pigmentosa

1- Refsum's disease.

2- Abetalipoproteinemia (Bassen Kornzweig syndrome).

3- MELAS mutation.

4- Kearns Sayre syndrome.

5- ATPase Subunit 6 Mutation (NARP).

6- Usher syndrome.

7- Leber Hereditary Optic Neuropathy (LHON).

8- Zellweger cerebrohepatorenal syndrome.

9- Laurence Moon Biedl syndrome (Bardet Biedl syndrome).

10- Flynn Aird syndrome.

11- Neonatal adrenoleukodystrophy.

12- Senior Loken syndrome.

13- Xp21.2-p21.3 microdeletion syndrome.

14- Rod-cone disease

15- Saldino Mainzer syndrome.

Patterns of intracranial calcification

1- Diffuse: as in congenital toxoplasmosis.

2- Periventricular: as in cytomegalovirus infection and calcified tubercles of tuberous sclerosis.

3- Occipitoparietal: as in Sturge Weber syndrome (tram track or railroad or serpentine).

4- Suprasellar: as in case of craniopharyngioma.

5- Basal ganglia calcification: as in hypoparathyroidism, pseudohypoparathyroidism (Albright hereditary osteodystrophy), MELAS mutation and Fahr syndrome (idiopathic basal ganglia calcification).

6- Symmetric calcification lateral to the sella in the medial temporal region: is pathognomonic to lipoid proteinosis (Urbach Weith syndrome) but is not present in all cases.

7- Ectopic calcification of the dura: in Papillon Lefevre syndrome.

8- Calcification of the falx cerebri: in Gorlin Goltz syndrome.

9- Fahr syndrome (idiopathic basal ganglia calcification).

Syndromes with cherry red spots of the macula

1- Tay Sachs disease.

2- Sandhoff disease.

3- Niemann Pick disease.

4- GM1 gangliosidosis.

5- Cherry red spot myoclonus syndrome (mucolipidosis I or Sialidosis type I).

6- Sialidosis type Π

7- May be present in Farber disease.

Syndromes associated with port wine stain (nevus flammeus)

1- Sturge Weber syndrome (encephalotrigeminal angiomatosis).

2- Klippel-Trenaunay-Weber syndrome.

3- Cobb syndrome (spinal arteriovenous malformation, port-wine stain).

4- Proteus syndrome.

5- Beckwith-Wiedemann syndrome.

6- Wyburn-Mason syndrome (Bonnet-Dechaume-Blanc syndrome).

Syndromes associated with hypocalcemia

1- Vitamin D dependant rickets.

2- DiGeorge's syndrome.

3- Shprintzen velocardiofacial syndrome.

4- Conotruncal anomaly face syndrome.

5- CATCH 22 spectrum.

6- Hungry bone syndrome.

7- Infantile osteopetrosis.

8- HDR (Barakat) syndrome.

9- X linked hypoparathyroidism.

10- Autosomal recessive hypoparathyroidism with dysmorphic features.

11- Autoimmune polyglandular syndrome type I.

12- Kearns-Sayre syndrome.

13- Hemochromatosis.

14- Wilson disease.

15- Albright hereditary osteodystrophy.

16- Rhabdomyolysis.

17- Tumor lysis syndrome.

18- Sanjad-Sakati syndrome.

19- Kenny-Caffey syndrome.

20- Pearson marrow pancreas syndrome.

Common acronyms used for pediatric syndrome associations

1-ABCD: ***A***lbinism, ***B***lack lock, ***C***ell migration disorder of the neurocytes of the gut and sensory neural ***D***eafness.

2- ACPS: ***A***cro ***C***ephalo ***P***oly ***S***yndactyly (Carpenter syndrome).

3- AEC: ***A***nkyloblepharon ***E***ctodermal dysplasia ***C***lefting (Hay Wells syndrome).

4-APECED: ***A***utoimmune ***P***oly***E***ndocrinopathy, ***C***andidiasis and ***E***ctodermal ***D***ysplasia.

5- AT: ***A***taxia ***T***elangiectasia.

6- ATR X: ***A***lpha ***T***halassemia, mental ***R***etardation, ***X*** linked.

7- BOR: ***B***ranchio ***O***to ***R***enal (Barakat syndrome).

8- 3C: ***C***ranio ***C***erebello ***C***ardiac dysplasia (Ritscher Schinzel syndrome).

9- CATCH 22: ***C***ardiac, ***A***bnormal facies, ***T***hymic hypoplasia, ***C***left palate, ***H***ypocalcemia, chromosome ***22*** deletion.

10- CAMFAK: ***C***ataract, ***M***icrocephaly, ***F***ailure to thrive, ***K***yphoscoliosis.

11- CFC: ***C***ardio ***F***acio ***C***utaneous.

12- CHARGE: ***C***oloboma, ***H***eart, ***A***tresia choanae, ***R***etardation, ***G***enital, ***E***ar.

13- CHILD: ***C***ongenital ***H***emidysplasia, ***I***chthyosiform erythroderma, ***L***imb ***D***efects.

14- CHIME: ***C***oloboma, ***H***eart, ***I***chthyosiform erythroderma, ***M***ental retardation, ***E***ar defects or ***E***pilepsy (Zunich Kaye syndrome).

15- CREST: ***C***alcinosis, ***R***ynaud's phenomena, ***E***sophageal dismobility, ***S***clerodactyly, ***T***elangiectasia.

16- CTAFS: ***C***onotruncal ***A***nomaly ***F***ace ***S***yndrome.

17- COA: ***C***ervico ***O***culo ***A***coustic (Wildervanck syndrome).

18- COACH: ***C***erebellar vermis hypoplasia, ***O***ligophrenia, congenital ***A***taxia, ***C***oloboma, ***H***epatic fibrosis.

19-DIDMOAD: ***D***iabetes ***I***nsipidus, ***D***iabetes ***M***ellitus, ***O***ptic atrophy, ***D***eafness (Wolfram syndrome).

20- DRESS: ***D***rug ***R***ash, ***E***osinophilia, ***S***ystemic ***S***ymptoms.

21- EEC: ***E***ctrodactyly, ***E***ctodermal dysplasia, ***C***left lip or palate.

22- FAVS: ***F***acio ***A***uriculo ***V***ertebral ***S***pectrum.

23- FCS: ***F***acio ***C***utaneo ***S***keletal (Costello syndrome).

24- GAPO: ***G***rowth retardation, ***A***lopecia, ***P***seudoanodontia (failure of tooth eruption), ***O***ptic atrophy.

25- HAM: ***H***ypoparathyroidism, ***A***ddison's disease, ***M***ucocutaneous candidiasis (type I autoimmune polyendocrinopathy).

26- HDR: ***H***ypocalcemia, ***D***eafness, ***R***etardation (Barakat syndrome).

27- HEC: ***H***ydrocephalus, ***E***ndocardial fibroelastosis, ***C***ataract.

28- ICF: ***I***mmunodeficiency, ***C***entromeric instability, ***F***acial abnormalities.

29- IMAGe: ***I***ntrauterine growth retardation, ***M***etaphyseal dysplasia, ***A***drenal hypoplasia, ***Ge***nital anomalies.

30- IPEX: ***I***mmune dysregulation, ***P***olyendocrinopathy, ***E***nteropathy, ***X*** linked.

31- KID: ***K***eratitis, ***I***chthyosis, ***D***eafness.

32- LAMB: ***L***entigines, ***A***trial myxomas, ***M***ucocutaneous myxomas, ***B***lue nevi (Carney complex).

33- LEOPARD: ***L***entigines, ***E***lectrocardiographic abnormalities, ***O***cular hypertelorism, ***P***ulmonary stenosis, ***A***bnormal genitals, growth ***R***etardation, sensorineural ***D***eafness.

34- MASA: ***M***ental retardation, ***A***phasia, ***S***huffling gate, ***A***dducted thumb.

35- MASS: ***M***itral valve prolapse, ***A***ortic dilatation, ***S***kin striae, ***S***keletal manifestations of Marfan syndrome.

36- MCA/MR: ***M***ultiple ***C***ongenital ***A***nomalies/***M***ental ***R***etardation syndrome.

37- MELAS: ***M***itochondrial ***E***ncephalomyopathy, ***L***actic ***A***cidosis, ***S***troke like episodes.

38- MERRF: ***M***itochondrial ***E***ncephalomyopathy, ***R***agged ***R***ed fibers.

39- MOMO: ***M***acrosomia, ***O***besity, ***M***acrocephaly, ***O***cular abnormalities.

40- MULIBREY NANISM: ***MU***scle, ***LI***ver, ***BR***ain, ***EY***e, ***NANISM***= dwarfism with congenital pericardial thickening and constriction.

41- NARP: ***N***europathy, ***A***taxia, ***R***etinitis ***P***igmentosa.

42- OAV: ***O***culo ***A***uriculo ***V***ertebral (Goldenhar syndrome).

43- ODD: ***O***culo ***D***ento ***D***igital.

44- OPD: ***O***culo ***P***alato ***D***igital.

45- OFD: ***O***ro ***F***acio ***D***igital (Mohr syndrome).

46- PAPA: ***P***yogenic ***A***rthritis, ***P***yoderma gangrenosum, ***A***cne.

47- PFAPA: ***P***eriodic ***F***ever, ***A***phthus stomatitis, ***P***haryngitis, ***A***denopathy (Marshal syndrome).

48-PHACE: ***P***osterior fossa anomalies, ***H***emangiomas, ***A***rterial anomalies, ***C***oarctation and other cardiac defects, ***E***ye abnormalities.

49- POEMS: ***P***olyneuropathy, ***O***rganomegaly, ***E***ndocrinopathy, ***M*** proteins, ***S***kin lesions (Crow-Fukase syndrome, Takatsuki disease, or PEP syndrome).

50- SADDAN: ***S***evere ***A***chondroplasia with ***D***evelopmental ***D***elay and ***A***canthosis ***N***igricans.

51- SCARF: ***S***keletal anomalies, ***C***utis laxa ***C***raniostenosis, ***A***bnormal genitals, ***R***etardation, ***F***acial abnormalities.

52- SHORT: ***S***hort stature, ***H***yperextensibility of joints or inguinal ***H***ernia, ***O***cular depression, ***R***ieger anomaly, ***T***eething delay.

53- SRP: ***S***hort ***R***ib ***P***olydactyly.

54- STORCH: ***S***yphilis, ***T***oxoplasmosis, ***O***thers, ***R***ubella, ***C***ytomegalovirus, ***H***erpes simplex.

55- TAR: ***T***hrombocytopenia ***A***bsent ***R***adius.

56- VACTERL: ***V***ertebral, ***A***nal, ***C***ardiac, ***T***racheo***E***sophageal, ***R***enal, ***L***imb anomalies.

57- VATER: ***V***ertebral, ***A***nal, ***T***racheo***E***sohageal, ***R***enal or ***R***adial.

58- VCFS: ***V***elo***C***ardio***F***acial ***S***yndrome.

59- WAGR /O: ***W***ilm's tumor, ***A***niridia, ***G***enital, ***R***etardation / ***O***besity.

60- WHIM: ***W***arts, ***H***ypogammaglobulinemia, ***I***nfections, ***M***yleokathexis.